UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

BEFORE THE HONORABLE ANTHONY J. BATTAGLIA, JUDGE PRESIDING
HONORABLE WILLIAM F. HIGHBERGER, JUDGE PRESIDING (JCCP)

IN RE INCRETIN-BASED THERAPIES PRODUCTS LIABILITY LITIGATION,	CASE NO. 13-MD-2452-AJB
AS TO ALL RELATED AND MEMBER CASES	SAN DIEGO, CALIFORNIA SEPTEMBER 11, 2015 9:02 A.M.

REPORTER'S TRANSCRIPT OF PROCEEDINGS
RE: MOTION HEARING

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SAN DIEGO, CALIFORNIA; FRIDAY, SEPTEMBER 11, 2015; 9:02 A.M.

DEPUTY CLERK: CALLING MATTER ONE ON CALENDAR, CASE NUMBER 13MD2452, IN RE INCRETIN MIMETICS PRODUCTS LIABILITY LITIGATION, ON FOR MOTION HEARING.

THE COURT: GOOD MORNING TO ALL OF YOU HERE, AND ON THE PHONE. AND WE ARE GOING TO ADDRESS, IN THE MDL, THE CROSS-MOTIONS FOR SUMMARY MOTION ON PREEMPTION; AND IN THE JCCP, THE DEFENDANTS' MOTION ON PREEMPTION GROUNDS IN A JOINT SESSION BY AGREEMENT OF COUNSEL.

WE HAVE YOUR SIGN-IN SHEETS FOR THOSE APPEARING IN COURT TODAY, AND WE'LL ATTACH THOSE TO THE RECORD RATHER THAN TAKING ROLL OVER A VERY LARGE GROUP. AND I HAVE A LIST OF COUNSEL THAT SIGNED UP FOR THE TELEPHONIC ATTENDANCE, AND WE'LL MAKE THAT EXHIBIT 2 TO THE RECORD, TO MEMORIALIZE THEIR PARTICIPATION. AND ALL OF THAT WILL SAVE US PROBABLY ABOUT TEN OR 15 MINUTES.

WITH THAT SAID, THE MATTERS BEING FULLY BRIEFED ON THE MERITS, WE'LL PROCEED AS PLANNED, WITH THE DEFENSE HAVING THE FIRST OPPORTUNITY TO ADDRESS ALL OF THE ISSUES TO THEIR SATISFACTION, HOPEFULLY WITHIN AN HOUR. AND THEN AFTER A BREAK WE'LL HEAR THE PLAINTIFFS' FIRST DISCUSSION OF THEIR VIEW OF THE ISSUES.

SO FROM THE DEFENSE SIDE, MR. HEARD, I THINK YOU WERE GOING TO START, SIR, SO YOU MAY PROCEED WHEN READY.

(EXHIBIT NOS. 1 AND 2 MARKED FOR IDENTIFICATION)

(EXHIBIT NOS. 1 AND 2 RECEIVED INTO EVIDENCE)

MR. HEARD: YOUR HONORS, THANK YOU VERY MUCH. MY INTENTION IS TO DEVOTE ABOUT 45 TO 50 MINUTES OF THIS FIRST HOUR, AND THEN ALLOW MR. GOETZ TO SPEAK TO SOME OF THESE ISSUES, AS WELL.

NEEDLESS TO SAY, I AM MINDFUL OF JUDGE HIGHBERGER'S TENTATIVE RULING THIS MORNING, ALTHOUGH HAVING ONLY A SHORT TIME TO LOOK AT IT. AND I AM KEEN TO ADDRESS JUDGE HIGHBERGER'S CONCERNS, BUT I'M GOING TO TRY TO DO SO WITHIN A BROADER FRAMEWORK, SINCE I DON'T KNOW FULLY THE QUESTIONS AND CONCERNS THAT JUDGE BATTAGLIA MAY HAVE ON THESE MOTIONS.

NEEDLESS TO SAY, THESE CROSS-MOTIONS FOR SUMMARY JUDGMENT HAVE BEEN AMPLY BRIEFED. WE'VE GOT SIX BRIEFS ON THIS CURRENT ROUND OF MOTIONS, AND THERE WERE ANOTHER SIX BRIEFS WHEN THE DEFENDANTS BRIEFED THIS EARLIER, AND THEN ASTRAZENECA BRIEFED IT. SO IT'S 12 BRIEFS. AND I THINK IT'S FAIR TO SAY THEY HAVE BEEN HIGHLY REPETITIVE IN THEIR ARGUMENTS.

SO I THOUGHT THIS MORNING WHAT WOULD BE MORE HELPFUL THAN SIMPLY A RUN THROUGH THOSE SAME ARGUMENTS, IS TO TRY TO ADDRESS FIVE QUESTIONS. FIVE QUESTIONS THAT SEEMS TO US PLAINTIFFS' ARGUMENT PUT TO US, THE DEFENDANTS, AND THAT WE NEED TO HAVE GOOD ANSWERS TO IF WE ARE TO BE ENTITLED TO PREVAIL ON THIS MOTION.

I AM GOING TO PUT THESE QUESTIONS IN TWO PLACES. AND I'M GOING TO COME BACK, OBVIOUSLY, TO THESE AS WE GO. BUT THEY

ARE ALSO ON THE SCREEN. AND THE FIRST ONE PERHAPS IS THE VEHICLE FOR ADDRESSING SOME OF JUDGE HIGHBERGER'S ELEMENTS OF HIS TENTATIVE RULING.

BUT THE QUESTION THERE IS WHAT REALLY IS THE TEST, AND IS THE CLEAR EVIDENCE TEST ARTICULATED BY THE SUPREME COURT. ONE THAT REQUIRES A CBE REJECTED BY THE FDA OR EFFECTIVELY REQUIRES THE SAME THING.

THE SECOND QUESTION -- AND, OBVIOUSLY, QUESTIONS ONE, TWO, AND THREE BEAR SOME RELATION TO ONE ANOTHER -- IS DOES THE FDA'S CONCLUSION THAT THE LABELING IS ADEQUATE AS TO PANCREATIC CANCER JUST ESTABLISH A FLOOR AND NOT A CEILING? IS IT IN SOME WAY GRADING THE LABELING WITH A GENTLEMAN'S C, AND ALLOWING FOR THE PROSPECT THAT ONE COULD DO A LOT BETTER?

I THINK THE THIRD QUESTION WE NEED TO ANSWER IS IS IT POSSIBLE THAT IF THE MANUFACTURER SUBMITTED A CBE, WOULD THE FDA DEFER TO IT? WOULD IT BE AN OCCASION TO RETHINK THE ISSUE? AND, THUS, WE WOULD NOT BE ENTITLED TO SUMMARY JUDGMENT ON PREEMPTION GROUNDS.

THE FOURTH QUESTION, OBVIOUSLY, IS RAISED IN PLAINTIFFS' BRIEF, AND THAT IS, WELL, IF THE FDA ALLOWED THE PANCREATITIS WARNING TO REMAIN IN THE LABELING, WHILE AT THE SAME TIME DECLARING THE LABELING TO BE ADEQUATE, DOES THAT SUGGEST THAT THEY WOULD RECONSIDER OR ALLOW A PANCREATIC WARNING ALONG THE SAME LINES?

AND THE LAST QUESTION IS, OBVIOUSLY, THERE ARE

ALLEGATIONS IN THIS LITIGATION THAT THE DEFENDANTS DID NOT DISCLOSE CERTAIN DATA TO THE FDA. AND SO IF THEY HAD THAT DATA, WOULD THEY STICK TO THIS CONCLUSION THAT THE LABELING IS ADEQUATE?

SO I'D LIKE TO ADDRESS EACH OF THOSE FIVE QUESTIONS IN TURN. AND PARTICULARLY IN ADDRESSING THE FIRST ONE, I WOULD LIKE TO SPEAK TO SOME OF JUDGE HIGHBERGER'S CONCERNS.

THE COURT: JUST SO YOU ARE ALL AWARE, I HAVEN'T ACTUALLY READ THE TENDERED RULING OR THE QUESTIONS, SO I'M A BLANK SLATE FOR YOUR PURPOSES. JUST SO THAT IS CLEAR.

MR. HEARD: SO THIS FIRST QUESTION IN OUR MIND REALLY HAS FOUR ASPECTS TO THE ANSWER, BRIEFLY STATED AS FOLLOWS: WE BELIEVE THE SUPREME COURT DID NOT ESTABLISH A SIMPLE BRIGHT-LINE TEST FOR ANSWERING THIS QUESTION. IT COULD EASILY HAVE DONE SO. IT COULD EASILY HAVE SAID WHAT YOU NEED AS A MATTER OF HISTORICAL FACT IS FOR THE MANUFACTURER TO HAVE SUBMITTED THE CBE AND FOR THE FDA TO HAVE REJECTED IT.

YET DESPITE ALL THE TALK IN THE *WYETH V. LEVINE* OPINION ABOUT CBES AND THEIR PLACE IN THE REGULATORY SCHEME, THE SUPREME COURT ENDED UP WITH A BROADER, IN A SENSE, A VAGUER TEST, AND THAT IS THE CLEAR EVIDENCE TEST. CLEAR EVIDENCE THAT THE FDA WOULD NOT HAVE APPROVED THE WARNING PROPOSED BY THE PLAINTIFFS.

THE NINTH CIRCUIT IN *GAETA*, WHICH WAS ONE OF THE VERY FIRST COURTS TO HAVE TO DEAL WITH THIS PROBLEM, YOU KNOW,

STATED AT THE BEGINNING OF ITS ANALYSIS: THE SUPREME COURT DID NOT DEFINE WHAT IS CLEAR EVIDENCE.

AND, VIRTUALLY, EVERY COURT SINCE HAS REPEATED THAT, MANTRA-LIKE, IN ITS OPINIONS. BUT THE COURT IN *GAETA* SAID WE CAN LEARN FROM WHAT THE SUPREME COURT SAID WAS INSUFFICIENT EVIDENCE.

AND WHAT IT SAID WAS INSUFFICIENT EVIDENCE IN THAT CASE -- IN ITS OWN CASE, AND WHAT IT PERCEIVED TO BE INSUFFICIENT IN *WYETH* WAS THERE WERE THREE PROBLEMS WITH BEING ABLE TO REACH A CONCLUSION THAT THE FDA WOULD HAVE REJECTED THE PROPOSED LABELING.

ONE IS THE SUPREME COURT SAID BUT THE FDA HAS GIVEN ONLY INTERMITTENT ATTENTION TO THIS SAFETY ISSUE OVER THE YEARS. IT'S NOT AT ALL CLEAR THAT THEY HAVE ANY CURRENT COMPREHENSIVE EVALUATION OF SCIENTIFIC EVIDENCE BEARING ON THIS SAFETY ISSUE IN FRONT OF THEM.

AND LAST OF ALL, THEY REALLY HAVEN'T MADE ANY CLEAR STATEMENT THAT THE LABELING IS ADEQUATE IN LIGHT OF THE SCIENTIFIC EVIDENCE ABOUT THE SAFETY ISSUE.

ABSENT THAT KIND OF EVIDENCE, HOW COULD WE POSSIBLY SAY THAT THE FDA WOULD HAVE REJECTED THE PLAINTIFFS' PROPOSED WARNING?

SO *GAETA* SAID THE INQUIRY IS NECESSARILY VERY CASE-SPECIFIC. WHAT HAS THE FDA DONE? WHAT HAS THE FDA SAID?

AND, JUDGE BATTAGLIA, IN DENYING OUR EARLIER MOTION

AS PREMATURE, YOU REAFFIRMED THAT WHAT WE HAVE IS IN A WAY A FACT-INTENSIVE ANALYSIS FOCUSED ON WHAT THE FDA HAS SAID AND DONE.

AND OUR SUBMISSION HERE IS THAT THE CLEAR EVIDENCE TEST IS MET BECAUSE WE HAVE A UNIQUE SET OF FACTS THAT SUPPLY THE VERY EVIDENCE THAT THE SUPREME COURT IN *WYETH*, AND THAT THE NINTH CIRCUIT IN *GAETA* SAID WE'RE MISSING.

WE HAVE EVIDENCE THAT THE FDA FOCUSED ON THE VERY SAFETY ISSUE AT HAND: PANCREATIC CANCER. WE HAVE EVIDENCE THAT THEY DID A COMPREHENSIVE EVALUATION OF THE SCIENTIFIC EVIDENCE BEARING ON THAT EXACT SAFETY ISSUE. AND WE HAVE A DECLARATION OF THE FDA ABOUT THE QUALITY OF THAT SCIENCE AND ABOUT THE ADEQUACY OF THE LABELING IN LIGHT OF THAT SCIENCE.

SO WE HAVE WHAT IS MISSING, AND WE HAVE IT IN RATHER UNPRECEDENTED FORM. BUT I WANT TO PREVIEW THIS: WE HAVE NOT ONLY FACTS THAT DISTINGUISH THIS CASE FROM ALL THE OTHERS, FACTS THAT WE WOULD SAY ARE UNIQUE IN DECLARING OR REVEALING THE FDA'S THINKING, BUT WE HAVE ADMISSIONS BY PLAINTIFFS VERY OWN EXPERT, ADMISSIONS THAT CONCEDE EVERY ELEMENT OF DEFENDANTS' CONTENTION ABOUT PREEMPTION. AND I WILL GET TO THOSE IN A MINUTE.

SO WE HAVE A MARRYING HERE OF FACTS WITH ADMISSIONS BY THE PLAINTIFFS' EXPERT THAT THERE IS CLEAR EVIDENCE ABOUT WHAT THE FDA WOULD DO.

FIRST, WHAT ARE THOSE UNIQUE FACTS? WELL, WE THINK

IT'S UNIQUE IN TERMS OF WHAT THE FDA DID, EFFECTIVELY SUBMIT A CBE TO ITSELF, BY ISSUING THE DRUG SAFETY COMMUNICATION IN 2013.

UNIQUE IN WHAT IT THEN DID, COLLABORATING WITH THE OTHER MAJOR REGULATORY AGENCY IN THE WORLD, THE EUROPEAN MEDICINES AGENCY, TO CONDUCT A YEAR-LONG STUDY OF ALL THE SCIENCE.

UNIQUE, THEN, IN TERMS OF ITS DECISION ABOUT HOW TO COMMUNICATE ITS CONCLUSIONS, NOT THROUGH PRIVATE COMMUNICATIONS WITH THE MANUFACTURERS, BUT THROUGH *THE NEW ENGLAND JOURNAL OF MEDICINE*, TO REACH THE BRIGHTEST POSSIBLE AUDIENCE OF DOCTORS AND PATIENTS AND BRING CLARITY TO THIS QUESTION OF WHETHER THERE WAS A GENUINE ISSUE WITH PANCREATIC CANCER.

AND LAST OF ALL, WE HAVE A VERY CLEAR STATEMENT OF THE FDA'S CONCLUSION IN *THE NEW ENGLAND JOURNAL OF MEDICINE.* WE HAVE BOTH THE CONCLUSION ABOUT THE QUALITY OF THE SCIENTIFIC EVIDENCE. THE EVIDENCE IS INCONSISTENT WITH ANY CLAIMS OF CAUSAL ASSOCIATION, BUT WE HAVE THE FDA SAYING THE LABELING IS ADEQUATE.

SO IF WE ENUMERATE WHAT WE THINK ADDS UP TO CLEAR EVIDENCE, HOW WOULD WE COUNT IT? WE WOULD SAY THERE IS SEVEN DISCRETE STATEMENTS OR ACTS THAT ADD UP TO THAT CLEAR EVIDENCE. AND I MEAN THAT WE'RE NOT TALKING JUST ABOUT ONE STATEMENT, SAID AT ONE POINT IN TIME: THE INDICATION THAT THE FDA THOUGHT THIS THROUGH, RETHOUGHT IT, RESTATED IT, AND ACTED IN

ACCORDANCE WITH IT.

NUMBER ONE, NOT SURPRISINGLY, *THE NEW ENGLAND JOURNAL OF MEDICINE*. IF WE HAD NOTHING ELSE, IT WOULD BE OUR POSITION THAT THAT ALONE IS CLEAR EVIDENCE OF THE FDA'S POSITION BECAUSE IT ENCAPSULATES ALL THE ELEMENTS THAT WERE MISSING IN *WYETH V. LEVINE*. IN *THE NEW ENGLAND JOURNAL OF MEDICINE*, WE KNOW THAT THE FDA HAS FOCUSED ON THE PRECISE ISSUE, PANCREATIC CANCER.

WE HAVE A RECITATION OF ALL IT DID OVER A PERIOD OF A YEAR WITH THE EMA TO EVALUATE THE SCIENTIFIC EVIDENCE.

AND LAST OF ALL, WE HAVE A CLEAR STATEMENT OF CONCLUSIONS BOTH ABOUT THE QUALITY OF THAT EVIDENCE AND ABOUT THE STATE OF THE LABEL, THAT IT'S ADEQUATE.

BUT THE FDA -- THAT'S NOT THE ONLY EVIDENCE WE HAVE. WE ALSO HAVE, A MONTH LATER, THE FDA'S REJECTION OF THE CITIZEN PETITION.

IN THAT PETITION, THE PETITIONERS SAY THAT THERE IS AN INCREASED RISK OF PANCREATIC CANCER IN THOSE TAKING VICTOZA. THE FDA REACHES OUT TO ADDRESS THIS QUESTION OF THE LABELING BECAUSE THE PETITIONERS ARE, AFTER ALL, SEEKING THE TOTAL WITHDRAWAL OF THE DRUG FROM THE MARKET.

AND IN REACHING OUT TO DISCUSS THE LABELING, THIS IS WHAT THE FDA SAYS, AGAIN: THE SCIENTIFIC EVIDENCE SHOWS US THAT THE CAUSAL ASSOCIATION WITH THE DRUG AND PANCREATIC CANCER IS INDETERMINATE. MOREOVER, THAT THE EVIDENCE SUBMITTED BY THOSE PETITIONERS, ADVERSE EVENT REPORTS, CONSTITUTES NO NEW

EVIDENCE THAT WOULD SUPPORT ANY CHANGES IN THE LABELING. AND PERHAPS MOST SIGNIFICANT OF ALL, THAT EVEN A SUSPICION OF CAUSAL ASSOCIATION IS INDETERMINATE.

NOW, DR. ALEXANDER FLEMING, THE PLAINTIFFS' EXPERT, SAYS ABOUT THIS RESPONSE: THIS IS EVEN STRONGER LANGUAGE THAN IN *THE NEW ENGLAND JOURNAL OF MEDICINE.* IT IS MORE POINTED; IT IS STRONGER.

SO THAT'S THE SECOND ELEMENT OF CLEAR EVIDENCE: THAT THE FDA RETURNS TO THIS QUESTION, REACHES OUT TO ADDRESS IT AND, IF ANYTHING, STATES AN EVEN STRONGER POSITION ABOUT THE ADEQUACY OF THE LABEL.

AND THEN, FIVE MONTHS LATER, THE FDA STAFF PREPARES A BRIEFING BOOK FOR THE ADVISORY COMMITTEE, WHICH IS GOING TO ADVISE THE FDA ON WHETHER TO APPROVE SAXENDA, YET ANOTHER DRUG IN THIS CLASS.

SO WE HAVE THE THIRD OCCASION WHEN THE FDA FOCUSES ON THIS ISSUE, MUSTERS THE SCIENTIFIC EVIDENCE, AND DECLARES A CONCLUSION, WHICH IS: LIRAGLUTIDE IS NOT MUTAGENIC, IT DOESN'T CAUSE MUTATIONS THAT CAUSE CANCER.

THE ANIMAL DATA, THE OBSERVATIONAL DATA, THE TRIAL DATA HAVE NOT SUPPORTED THE CAUSAL ASSOCIATION. AND BEYOND THAT, THIS REMAINS A HYPOTHESIS NOT PROVEN. THE STUDIES HAVE BEEN INCONCLUSIVE. THEY DO NOT SUPPORT PANCREATIC CANCER AS A DRUG-RELATED RISK.

SO THE REJECTION OF THIS -- I MEAN, PRESENTATION OF

THIS BRIEFING BOOK GIVES US THE THIRD PIECE OF CLEAR EVIDENCE, THE THIRD TIME WITHIN A SIX-MONTH PERIOD THAT THE FDA HAS DONE ALL THREE THINGS: FOCUSED ON THE ISSUE, MUSTERED THE SCIENTIFIC EVIDENCE, AND DECLARED ITS CONCLUSION ABOUT THE ADEQUACY OF THE LABEL.

AND THEN WHAT I WOULD POINT TO AS THE FOURTH, FIFTH, SIXTH, AND SEVENTH ITEMS OF CLEAR EVIDENCE IS THAT DURING THIS PERIOD FROM FEBRUARY 2014 UNTIL MARCH OF 2015, THE FDA, FOUR TIMES, APPROVES DRUGS IN THIS CLASS WITHOUT A PANCREATIC CANCER WARNING.

IF THOSE APPROVALS STOOD APART FROM ALL THESE OTHER ANALYSIS AND STATEMENTS, MAYBE IT WOULD NOT MEAN MUCH. BUT HERE, UNDER A REGULATORY REGIME, WHICH NOW ALLOWS THE FDA TO MANDATE LABELING, WE HAVE ACTION CONSISTENT WITH THE FDA'S STATEMENTS.

THESE SEVEN STATEMENTS, COUPLED TOGETHER IN A SHORT TIME PERIOD, WE SAY CONSTITUTE AS CLEAR EVIDENCE AS ONE COULD POSSIBLY HAVE OF WHAT THE FDA WOULD DO IF CONFRONTED WITH A PANCREATIC CANCER WARNING REQUEST.

NOW, I SAID THESE UNIQUE FACTS ARE COUPLED WITH -- AND THIS IS CERTAINLY IN NO CASE IN THE REPORTED DECISIONS -- ADMISSIONS BY PLAINTIFFS' EXPERTS THAT WE SAY CONFIRM EVERY STEP OF OUR CLAIM.

DR. FLEMING. DR. FLEMING CONCEDES, FIRST, THAT ONE OF THE REASONS THAT THE FDA UNDERTOOK THIS COMPREHENSIVE

EVALUATION OF THE SCIENTIFIC EVIDENCE WAS TO CONSIDER THE ADEQUACY OF THE PACKAGE INSERTS AS THEY RELATED TO PANCREATIC CANCER. HE ACKNOWLEDGES THAT.

DR. FLEMING ACKNOWLEDGES THAT THE YEAR-LONG INVESTIGATION OF THE SCIENTIFIC EVIDENCE THAT THE FDA CONDUCTED WAS A VERY ROBUST EVALUATION, NOT SOME HAND-WAVING EXERCISE, NOT SOME CURSORY SUPERVISION ONE, BUT ONE THAT WAS ROBUST.

DID THEY LOOK CAREFULLY AT THE DATA? THERE IS NO DOUBT THAT THEY DID SO. WERE THEY TAKING THIS SERIOUSLY? HE HAS NO DOUBT ABOUT THAT FACT.

DR. FLEMING FURTHER CONCEDES THAT THIS WAS AN UNPRECEDENTED COLLABORATION WITH THE EMA AND AN UNPRECEDENTED DECISION TO PUBLISH IN *THE NEW ENGLAND JOURNAL OF MEDICINE*.

AND DR. FLEMING SAYS AND ACKNOWLEDGES THAT THE CONCLUSION THAT THE FDA REACHED WAS A CONCLUSION AND DETERMINATION BY THE FDA THAT THE LABELING WAS ADEQUATE.

SO IT WAS LOOKING AT THE LABELING, IT WAS A SERIOUS SCIENTIFIC INVESTIGATION, IT DECIDED THAT THE LABELING WAS ADEQUATE, IT WAS UNPRECEDENTED IN ITS COMMUNICATION.

BUT LET'S LOOK AT SOME FURTHER ADMISSIONS ON THIS SCORE. AND I'M GOING TO TURN NOW TO ACTUAL VIDEO CLIPS. DR. FLEMING ACKNOWLEDGES THAT THIS IS AN UNPRECEDENTED CONCLUSION.

(PLAYING VIDEO)

AND DR. FLEMING ACKNOWLEDGES THAT THE FDA CONCLUDED

THAT THE SCIENTIFIC EVIDENCE DID NOT MEASURE UP TO THE REGULATORY STANDARD FOR INCLUDING WORDING IN THE WARNING SECTION OF THE LABELING.

(PLAYING VIDEO)

AND DR. FLEMING ACKNOWLEDGES THAT IF ONE CONSIDERS WHETHER THE SCIENTIFIC EVIDENCE MEASURES UP TO THE STANDARD FOR INCLUSION IN THE ADVERSE REACTIONS SECTION OF THE LABELING, THAT THE FDA CONCLUDED THAT THE SCIENTIFIC EVIDENCE DOES NOT MEASURE UP.

(PLAYING VIDEO)

AND DR. FLEMING GOES AND ALSO STATES THAT UNDER THESE CIRCUMSTANCES THERE IS NO PRECEDENT FOR THE FDA APPROVING A CBE UNDER THESE CIRCUMSTANCES.

(PLAYING VIDEO)

I PREVIEWED THAT SLIDE WRONG. HE CONCEDES THAT THIS IS THE OFFICIAL POSITION OF THE FDA EVEN THOUGH PLAINTIFFS CONTEST THAT IN THEIR BRIEFING.

NOW, IN THIS NEXT CLIP HE SAYS IT WOULD BE UNPRECEDENTED FOR THE FDA TO APPROVE A CBE UNDER THESE CIRCUMSTANCES. (PLAYING VIDEO)

AND LAST, DR. FLEMING CONCEDES THAT WHERE THE FDA HAS STUDIED THE ISSUE, DETERMINED THE SCIENTIFIC EVIDENCE INADEQUATE, CONCLUDED THAT A LABELING IS ADEQUATE ITSELF, IT WOULD BE, TO USE HIS WORD, ABSURD TO THINK THAT THE FDA WOULD THEN APPROVE A PANCREATIC CANCER WARNING.

(PLAYING VIDEO)

SO IF THERE IS EVER A CASE WHERE THE EVIDENCE MEASURES UP TO WHAT WAS MISSING IN *WYETH V. LEVINE*, AND MEASURES UP IN TO *GAETA*, IT IS SURELY THIS CASE, WHERE THE FDA SPOKE NOT ONCE, BUT THREE TIMES. IT'S A CONFIRMATORY ACTION FOUR TIMES BY APPROVING LABELING IN THIS TIME PERIOD.

WHERE THE FDA'S CONCLUSION WAS STRONGER EACH TIME IT SPOKE, AND WHERE PLAINTIFFS' EXPERT AGREES THAT THE SCIENTIFIC EVIDENCE, IN THE FDA'S VIEW, DOES NOT MEASURE UP TO THE STANDARD FOR INCLUSION IN THE WARNINGS OR INCLUSION IN THE ADVERSE REACTION SECTION OF LABELING, THE ONLY TWO WARNING SECTIONS WHERE THEY HAVE EVER SUGGESTED THAT A WARNING MIGHT BE PLACED.

WE CAN NEVER BE ABSOLUTELY SURE, I SUPPOSE, IN ANY CASE, BUT THAT WAS NOT THE TEST THE FDA PUT. IT DID NOT PUT A HISTORICAL TEST OF "CAN WE SAY FOR A MATTER OF HISTORICAL FACT THAT THE EXACT WARNING HAS BEEN PRESENTED TO THE FDA AND IT HAS REJECTED IT?"

THE QUESTION WAS A WOULD-HAVE TEST. LOOKING AT ALL THE EVIDENCE, CAN WE SAY CLEARLY ENOUGH THAT THE FDA WOULD HAVE REJECTED A WARNING? AND WE SAY THAT WHAT WE HAVE HERE CLOSELY COUPLED IN TIME IS THE FOCUS ON THE ISSUE, THE COMPREHENSIVE EVALUATION OF THE EVIDENCE, A CONCLUSION BY THE FDA THAT THE LABELING IS ADEQUATE IN LIGHT OF THE SCIENTIFIC EVIDENCE BECAUSE IT DOES NOT MEASURE UP TO THE REGULATORY STANDARD, AND

SAID REPEATEDLY OVER A 14-MONTH PERIOD, AND ACTED UPON IT.

WITH PLAINTIFFS' EXPERT CONCEDING AT THE END OF THE DAY, IT WOULD BE ABSURD TO THINK THAT GIVEN THIS COMBINATION OF FACTS, THAT THE FDA WOULD TURN AROUND AND APPROVE A PANCREATIC CANCER WARNING.

NOW, IF THAT DOES ADD UP TO CLEAR EVIDENCE, WHAT CLAIMS ARE PREEMPTED? AND I WANT TO ADDRESS HERE JUDGE HIGHBERGER'S VIEW THAT EVEN IF IT WERE THE CASE THAT WE KNOW WHAT THE FDA THINKS NOW, THAT WOULD NOT NECESSARILY PREEMPT CASES THAT AROSE, ALLEGED FAILURES TO WARN THAT TOOK PLACE IN 2006 OR '8' OR '10.

PROBABLY THREE ANSWERS HERE. THE FIRST, IF WE SIMPLY LOOK TO THOSE CASES WHERE PREEMPTION HAS BEEN GRANTED IN WHOLE OR IN PART, INVARIABLY THE FACTS ARE THAT THE COURT FINDS CLEAR EVIDENCE OF WHAT THE FDA WOULD DO, FOR EXAMPLE IN 2008, AND ON THAT BASIS FINDS THAT THE PLAINTIFFS' CLAIM, WHICH AROSE IN 2003, IS PREEMPTED. OR THAT ACTIONS TAKEN IN 2006 AND 2008, TO DESCRIBE ANOTHER CASE, PREEMPT A CAUSE OF ACTION THAT AROSE THREE OR FIVE YEARS EARLIER.

THE COURT: AND FOR YOUR PURPOSES FOR YOUR ARGUMENT, AROSE MEANING WHAT? DIAGNOSED, OR SOMETHING ELSE?

MR. HEARD: WHAT'S RELEVANT HERE IS THE POINT AT WHICH THE PLAINTIFF INITIATED USE OF THE DRUG, HAD AN EXCHANGE WITH THE DOCTOR -- HE EITHER READ THE LABELING HIMSELF OR HERSELF -- AND THE DOCTOR WAS IN A POSITION TO WARN. AND

ACCORDING TO PLAINTIFFS' ALLEGATION, FAILED TO WARN APPROPRIATELY BECAUSE THEY DIDN'T HAVE A LABEL THAT GAVE THEM A PROPER WARNING.

JUDGE HIGHBERGER: AS I UNDERSTAND THE FACTS OF THE *DOBBS* CASE, THE ACTUAL REJECTION BY THE FDA CAME LATER IN TIME THAN THE PLAINTIFFS' EXPOSURE TO THE DRUG. SO THAT FITS YOUR ANALYTICAL CONSTRUCT.

IS THERE ANOTHER PUBLISHED CASE THAT HAS THE SAME FACTORS?

MR. HEARD: WELL, THE THREE CASES I WOULD CITE THE COURT TO ON THIS, FIRST, IS A DECISION OF THE SEVENTH CIRCUIT.

JUDGE HIGHBERGER: THEY ARE, I AM PRESUMING, IN YOUR BRIEF?

MR. HEARD: THIS ONE IS NOT. *ROBINSON V. MCNEIL.*

JUDGE HIGHBERGER: *ROBINSON V. MCNEIL.*

MR. HEARD: 615 F3D 861, DECIDED IN 2010.

A MORE RECENT CASE ON THE SAME SET OF FACTS -- THAT IS, SAME DRUG, SAME SET OF FDA ACTIONS -- IS *RECKIS V. JOHNSON & JOHNSON*. THIS WAS A DECISION IN APRIL OF THIS YEAR BY THE MASSACHUSETTS SUPREME JUDICIAL COURT. 28 NORTHEAST 3RD 445.

AND MOST RECENT OF ALL, *RHEINFRANK V. ABBOTT*. IT'S ONLY REPORTED IN WESTLAW AT THIS POINT, I BELIEVE. 2015 WESTLAW 4743056, THE SOUTHERN DISTRICT OF OHIO, DECIDED ON AUGUST THE 10TH, GRANTING PREEMPTION ONLY IN PART. BUT, AGAIN, PREEMPTION RELATES BACK TO AN EARLIER TIME WHEN THE PLAINTIFF

TOOK THE DRUG AND SUFFERED THE INJURY.

NOW, I WILL COME BACK TO THIS CASE LATER BECAUSE THIS IS A CASE IN WHICH THE COURT, IN EFFECT, ADOPTS JUDGE BATTAGLIA'S REASONING ON THE FRAUD ON THE FDA ALLEGATIONS AND FINDS THOSE IRRELEVANT TO THE PREEMPTION INQUIRY.

SO MY FIRST ANSWER, JUDGE HIGHBERGER, IS I THINK THE CASES, WHEN THEY HAVE APPLIED A PREEMPTION RULING, HAVE APPLIED IT BACK IN TIME, AND THAT THEY HAVE DONE SO ON THIS PRINCIPLE, WHICH IS REFLECTED IN THE *RHEINFRANK* CASE REASONING, I BELIEVE. WHICH IS IF THE FDA FINDS THE SCIENTIFIC EVIDENCE INADEQUATE AT THIS POINT IN TIME, THAT IT'S HIGHLY UNLIKELY THAT THEY WOULD HAVE APPROVED A WARNING ON LESSER SCIENTIFIC EVIDENCE AT EARLIER STAGES IN THE GAME.

BUT THERE IS ALSO THIS THIRD VERY PRACTICAL ASPECT. WELL, THE THIRD PRACTICAL ASPECT IS THERE HAS NEVER BEEN A QUESTION RAISED IN THE BRIEFING THAT A PREEMPTION RULING WOULDN'T AFFECT ALL THE PLAINTIFFS. THE PLAINTIFFS HAVE NEVER ARGUED DIFFERENTLY.

AND, IN FACT, WHAT IS IMPLICIT IN THE ARGUMENT IS THAT IF THE MANUFACTURERS HAD SUBMITTED A CBE AND THE FDA HAD REJECTED IT, IF WE HAD A REJECTION OF THE CBE IN FEBRUARY OF 2014 INSTEAD OF AN ARTICLE IN *THE NEW ENGLAND JOURNAL OF MEDICINE*, THERE HAS NEVER BEEN ANY DOUBT ON THE PLAINTIFFS' SIDE THAT THAT WOULD ESTABLISH THEIR VIEW OF HOW THE PREEMPTION TEST IS MET AND THAT WOULD PREEMPT THE PLAINTIFFS' CLAIMS.

SO AS A MATTER OF WHAT'S BEEN ARGUED, AND AS A MATTER OF WHAT THE COURTS HAVE RULED, WE TAKE ISSUE, RESPECTFULLY, WITH THAT CONCLUSION.

SO LET ME COME BACK TO THIS ISSUE, NECESSARILY, OF WHETHER THERE IS CLEAR EVIDENCE IN DIFFERENT FRAMEWORKS. BUT LET ME TURN NOW TO THE SECOND QUESTION: IF SOMEHOW THE DECLARATION THAT THE LABELING IS ADEQUATE IS SORT OF A WEAK BLESSING.

AND I THINK HERE IT'S IMPORTANT TO RECOGNIZE THAT WHEN WE SAY THAT THE LABELING IS ADEQUATE, WE ARE NOT QUITE USING THAT TERM IN THE WAY WE WOULD IF WE WERE ON THE STREET AND IT WAS COMMON PARLANCE, WHERE ADEQUATE MAY JUST MEAN, YOU KNOW, SORT OF OKAY.

IN THIS FRAMEWORK, OF COURSE, IF THE LABELING IS ADEQUATE, DEFENDANTS ARE ENTITLED TO SUMMARY JUDGMENT ON THE FAILURE-TO-WARN CLAIM. IF THE LABELING IS INADEQUATE, THEN THE PLAINTIFFS HAVE PROVEN NEGLIGENT FAILURE TO WARN. SO ADEQUATE IS A MUCH MORE BLACK-AND-WHITE CONCEPT APPLIED IN THIS CONTEXT.

BUT MORE IMPORTANTLY, THE BOTTOM LINE POINT IS LABELING IS GOVERNED BY REGULATORY STANDARDS. AND THOSE REGULATORY STANDARDS, WHICH ARE CONTAINED IN SECTION 201.57(C), ARE SCIENCE-BASED STANDARDS THAT DEPEND ON THE QUANTUM AND QUALITY OF THE SCIENTIFIC EVIDENCE PUT FORWARD IN SUPPORT OF ANY LABELING LANGUAGE.

JUDGE HIGHBERGER: ISN'T THIS ARGUMENT TRYING TO

IMPLIEDLY SAY THAT IF THE FDA APPROVES THE LABEL, A STATE LAW FAILURE-TO-WARN THEORY NECESSARILY MUST FAIL?

MR. HEARD: NO. THAT CLEARLY WAS THE ARGUMENT THAT WYETH MADE IN *WYETH V. LEVINE*. AND WYETH WANTED TO ARGUE THAT THE FDA'S INITIAL APPROVAL OF THE LABELING MADE THAT SORT OF LABELING ADEQUATE FOR ALL TIME.

IF WE LOOK AT THAT LANGUAGE, WYETH'S ARGUMENT -- AND HERE IS THE SUPREME COURT COMMENTING ON THIS ARGUMENT BY *WYETH*. *WYETH* SAYS IT ESTABLISHES BOTH A FLOOR AND A CEILING. AND THE FDA SAYS REALLY? REGARDLESS OF WHETHER THERE IS ANY EVIDENCE THAT THE FDA HAS CONSIDERED THE STRONGER WARNINGS AT ISSUE?

NO, THE SUPREME COURT SAYS, NOT REGARDLESS. IT'S CRUCIALLY IMPORTANT TO KNOW WHETHER THE FDA HAS CONSIDERED THE STRONGER WARNING AND THE MOST UP-TO-DATE SCIENTIFIC EVIDENCE. THUS, ITS HOLDING THAT THE INITIAL APPROVAL OF THE LABELING DOESN'T ESTABLISH A FLOOR AND A CEILING; IT HAS TO BE A DETERMINATION THAT THE LABELING IS ADEQUATE IN LIGHT OF THE CURRENT SCIENCE AND A FOCUS ON THE SAFETY QUESTION AT HAND.

SO WHAT I'M SAYING HERE IS THE SUPREME COURT, IN FACT, DIRECTS US TO ASK: IS THE FDA LOOKING AT THE SCIENTIFIC EVIDENCE? AND IT'S IMPERATIVE THAT THEY DO BECAUSE THE REGULATORY STANDARD FOR LABELING IS SCIENCE-BASED. AND IT'S THE SAME STANDARD WHETHER IT'S A MANUFACTURER SEEKING INITIAL LABELING OR REVISED LABELING. AND IT'S THE SAME STANDARD WHETHER THE FDA IS APPROVING THE INITIAL LABELING, APPROVING A

CBE, OR ITSELF MANDATING LABELING, AS IT NOW HAS THE POWER TO DO.

SO WHERE THE FDA CONCLUDES THAT THE SCIENCE DOES NOT SUPPORT ANY CHANGE TO THE PANCREATIC CANCER WARNING, IT IS APPLYING A SET STANDARD.

NOW, LET'S JUST LOOK QUICKLY AT HOW IMPORTANT THIS QUESTION OF SCIENCE IS.

JUDGE HIGHBERGER: BUT, THEREFORE, YOU ARE SAYING THAT IF THE FDA HAS STUDIED THE LABEL, ITS APPROVAL OF IT NECESSARILY IMPEDES ANY STATE LAW CLAIM?

MR. HEARD: YES. WE ARE SAYING IF THE FDA FOCUSED ON THE SAFETY ISSUE AND ON THE SCIENCE, AND IT THEN CONCLUDES THAT THE LABELING IS ADEQUATE, THAT'S PRECISELY THE CLEAR EVIDENCE THAT ADDS UP TO PREEMPTION.

JUDGE HIGHBERGER: BUT THEY DON'T HAVE TO REJECT A CBE; THEY JUST HAVE TO DECLARE A LABEL AT A CURRENT POINT IN TIME IS ADEQUATE? AND THAT IS ENOUGH TO DEFEAT THE STATE LAW CLAIM THAT OTHERWISE HAS COME DOWN OVER THE DECADES?

MR. HEARD: JUST TO MAKE ABSOLUTELY SURE I'M BEING CLEAR ON THIS POINT, WE ARE SAYING WHAT HAS TO BE COUPLED TOGETHER IS BOTH THE FDA'S EVALUATION OF THE CURRENT SCIENCE, AND THE STATEMENT THAT THE LABELING IS ADEQUATE.

I THINK THIS IS WHAT WAS HAPPENING IN THIS CASE, AND MUCH OF WHAT THE SUPREME COURT PERCEIVED WAS A STATEMENT BY THE FDA THAT THE LABELING IS ADEQUATE. THAT IS SORT OF IN THE AIR,

MAY NOT BE WORTH VERY MUCH.

BUT OUR CONTENTION HERE IS THAT THE FDA'S STATEMENTS THAT THE LABELING IS ADEQUATE IS AT ALL TIMES TETHERED TO ITS EVALUATION OF THE SCIENTIFIC EVIDENCE, TO THIS EVALUATION THAT IT DID WITH THE EMA FOR A PERIOD OF A YEAR. YOU KNOW, AN EVALUATION IN WHICH IT SAYS WE'VE REVIEWED 250 TOXICOLOGY STUDIES WITH 18,000 ANIMALS, WE'VE REQUIRED THE MANUFACTURERS TO DO SOME SHORT-TERM ADDITIONAL ANIMAL STUDIES, WE'VE HAD INDEPENDENT PATHOLOGISTS RE-EXAMINE OVER 100 HISTOPATHOLOGY SLIDES, WE'VE LOOKED AT MORE THAN 200 CLINICAL TRIALS AND FOUND NO CONCLUSION OF A STATISTICALLY SIGNIFICANT INCREASED RISK. WE'VE LOOKED AT TWO CARDIOVASCULAR OUTCOME TRIALS, WHICH HAVE PANCREATIC CANCER OUTCOMES. IN ONE OF THEM THERE IS NO PANCREATIC CANCERS IN EITHER ARM OF THE STUDY. IN THE OTHER ARM, THERE IS TWICE AS MANY CANCERS IN THE PLACEBO ARM THEN IN THE STUDY. WE'VE LOOKED AT ALL OF THAT.

AND THEIR DECLARATION ABOUT THE ADEQUACY OF THE LABEL IS TETHERED TO THAT ANALYSIS OF THE SCIENCE.

THE COURT: SO TO BE OVERLY SIMPLISTIC, YOU ARE DISTINGUISHING BETWEEN A MANUFACTURER SUBMITTING A DRUG AND A PROPOSED LABEL FOR INITIAL APPROVAL?

MR. HEARD: YES.

THE COURT: AND THE SITUATION WHERE THE FDA, IN ITS OWN REGARD, HAS MADE A SOMEWHAT SEPARATE OR A STUDIED INQUIRY BEYOND THE DATA SIMPLY SUBMITTED BY THE MANUFACTURER?

MR. HEARD: YES. BECAUSE IN ALMOST EVERY CASE, OF COURSE, THESE CLAIMS ARISE WELL AFTER THIS INITIAL APPROVAL OF THE LABELING. AND I THINK THE SUPREME COURT RIGHTLY ASKS. WE CAN ONLY RIDE THAT INITIAL APPROVAL SO FAR, IF THERE IS A REASON TO BELIEVE THERE IS ADDITIONAL SCIENTIFIC EVIDENCE THAT OUGHT TO BEAR ON WHETHER THERE SHOULD BE A REVISED LABELING.

SO THIS STATES THE OBVIOUS. BUT IT'S HERE BECAUSE IT TAKES US BACK 35 YEARS OF THE FDA PUTTING AN EMPHASIS ON THE FACT THAT ALL LABELING STATEMENTS MUST BE SUPPORTED BY SCIENTIFIC EVIDENCE; THAT IT'S SCIENTIFICALLY ACCURATE INFORMATION THAT GETS INCLUDED IN THE LABELING; AND THAT THE FDA IS GOING TO SCRUTINIZE CAREFULLY ANY LABELING CHANGE, NO MATTER WHERE IT CAME FROM.

NOW, THE CBE IS A NARROW EXCEPTION, BUT LET'S BE CLEAR. IT'S NOT A NARROW EXCEPTION TO THE STANDARD BASED ON SCIENTIFIC EVIDENCE. IT'S AN EXCEPTION ONLY INSOFAR AS LABELING CAN BE PUT INTO EFFECT WITHOUT PRIOR FDA APPROVAL.

WHAT THE SECOND BULLET TELLS US IS THAT CBE SUPPLEMENTS MAY ONLY BE USED IF THERE IS SUFFICIENT EVIDENCE OF A CAUSAL ASSOCIATION. AND THE FDA HAS SAID SUFFICIENT EVIDENCE IS A REFERENCE TO THE STANDARDS IN 201.57(C)(6) AND (C)(7).

AND, BY THE WAY, BECAUSE I HAD TO ASK THIS QUESTION AND BE REMINDED AGAIN LAST NIGHT, A CBE-0 IS A CBE THAT CAN BE PUT INTO EFFECT IMMEDIATELY, ZERO DAYS. AND THERE IS A CBE-30 THAT WOULD REQUIRE A 30-DAY WAIT.

THE COURT: IS THERE A DISTINCTION WITH A DIFFERENCE BETWEEN SUFFICIENT EVIDENCE AND CLEAR EVIDENCE FOR THIS ANALYSIS OF THE DEFENDANTS' POSITION?

MR. HEARD: WELL, THE DIFFERENCE IS THIS: THE CLEAR EVIDENCE GOES TO WHAT WOULD THE FDA DO. SUFFICIENT EVIDENCE GOES TO WHETHER THE SCIENCE WARRANTS REVISED LANGUAGE.

SO WE'RE SAYING HERE WE KNOW WHAT THE FDA HAS CONCLUDED. THAT'S CLEAR. AND THE CONCLUSION THAT THE FDA HAS REACHED IS BASED ON A DETERMINATION ABOUT WHETHER THE SCIENCE IS SUFFICIENT.

AND IN A PREEMPTION INQUIRY, THE QUESTION FOR THE COURT IS NOT WHETHER THE FDA IS RIGHT OR WRONG; IT'S SIMPLY WHETHER WE CAN BE CERTAIN THAT WE KNOW WHAT THE FDA -- OR WE CAN BE CLEAR ABOUT WHAT THE FDA WOULD DO.

SO, AGAIN, THE IMPORTANT POINT HERE IS IT'S A UNIFORM SET OF STANDARDS. IT'S NOT A DIFFERENT STANDARD FOR CBES AS OPPOSED TO INITIAL LABELING OR EVEN FDA-MANDATED LABELING THAT COMES DOWN THE LINE.

IF YOU MEET THAT STANDARD OF EVIDENCE, THEN A CBE SUBMISSION IS APPROPRIATE. IF THE CBE SUBMISSION DOESN'T MEET THAT STANDARD OF EVIDENCE, IT'S NOT APPROPRIATE.

SO WHERE DOES THAT TAKE US? IT TELLS US THAT IF WE GO BACK TO THE QUESTION HERE, YOU KNOW, IS THERE A FLOOR OR A CEILING, OR IS THE FDA GOING TO DEFER, THE FDA HAS A STANDARD TO APPLY. IT'S A SCIENCE-BASED STANDARD. WE KNOW HOW IT'S

APPLIED IT. IT'S CLEAR HOW IT'S APPLIED IT; AND, THEREFORE, PREEMPTION IS APPROPRIATE.

NOW, THAT LEAVES ONLY ONE SORT OF PERIPHERAL POINT HERE. I THINK IT LEAVES THE PLAINTIFFS SAYING -- I FIND IT IMPLICIT IN THEIR BRIEFS, GIVEN DR. FLEMING'S CONCESSIONS THAT THE FDA DETERMINED THAT THE SCIENCE DOESN'T MEET THE THRESHOLD FOR BEING IN THE WARNINGS OR THE ADVERSE REACTIONS. WHAT ARE THEY LEFT TO SAY?

THEY ARE LEFT TO SAY THAT THE SAFETY SIGNAL STANDING ALONE, THE SAFETY SIGNAL THAT GAVE RISE TO THE 2013 DRUG SAFETY COMMUNICATION, MUST BE SOME EVIDENCE OF CAUSAL ASSOCIATION, AND THE SAFETY SIGNAL BELONGS IN THE LABELING.

BUT THE FDA HAS BEEN QUITE CLEAR THAT HYPOTHETICALS, THEORETICAL SUGGESTIONS DO NOT BELONG IN THE LABELING. THE FDA HAS PREVIOUSLY FOUND THAT LABELING THAT INCLUDES THEORETICAL HAZARDS CAUSES PROBLEMS WITH THE DOCTOR'S ABILITY TO ABSORB AND ACT ON MEANINGFUL RISK INFORMATION.

AND DR. FLEMING AGREES -- I'M SORRY. ONE SECOND.

DR. FLEMING AGREES THAT A SAFETY SIGNAL IS MERELY A HYPOTHESIS. A HYPOTHESIS NECESSARILY WARRANTS INVESTIGATION, BUT HERE THE FDA DID THE INVESTIGATION, IT REPORTED ITS CONCLUSIONS, IT CONFIRMED THEM TWICE, IT ACTED ON THEM FOUR MORE TIMES.

AND REMEMBER WHAT THE FDA SAID, IN REJECTING THE CITIZEN PETITION -- THAT LANGUAGE ABOUT SUSPICION. EVEN A

SUSPICION IS INDETERMINATE AT THIS TIME. SO AFTER ITS YEAR-LONG INVESTIGATION, IT SAYS, ESSENTIALLY, EVEN THE SAFETY SIGNAL IS INCONCLUSIVE AND INDETERMINATE.

SO THE ANSWER TO MY SECOND QUESTION IS NO, FOR THOSE REASONS.

THE THIRD QUESTION, ASKED IN A SLIGHTLY DIFFERENT WAY: IS IT POSSIBLE THAT THE FDA WOULD JUST RETHINK THIS ISSUE BECAUSE IT'S BEING ASKED TO RETHINK IT BY THE MANUFACTURER, AND THE MANUFACTURER IS RESPONSIBLE FOR THE LABEL AND SOMETIMES THE MANUFACTURER HAS DATA THE FDA DOESN'T?

NOT AN UNREASONABLE QUESTION BUT, OF COURSE, THERE IS NO DEFERENCE TO THE MANUFACTURER IN THE LABELING. IN ALL OF THE MATERIAL WE JUST EXAMINED, THE FDA IS APPLYING A STANDARD. AND WE KNOW HOW THE FDA HAS APPLIED THE STANDARD AND THAT IT FINDS THE SCIENTIFIC EVIDENCE DOES NOT MEET THE STANDARD, AND THAT DR. FLEMING AGREES THAT THE FDA HAS FOUND, UNEQUIVOCALLY, THAT THE SCIENCE DOESN'T MEET THE STANDARD.

AND THE FDA HAS SAID THAT NOT ONCE, BUT TO BEAT A DEAD HORSE, IT HAS SAID IT THREE TIMES, STRONGER EACH TIME. IN THE BRIEFING BOOK, OF COURSE, IT'S SAYING THIS IS HYPOTHESIS, NOT YET PROVEN; THE ANIMAL, THE OBSERVATIONAL, THE CLINICAL TRIAL DATA ALL DO NOT SUPPORT A CAUSAL ASSOCIATION.

SO WOULD THE FDA SIMPLY DEFER BECAUSE IT'S THE MANUFACTURER? DR. FLEMING ANSWERS THAT BY SAYING IT'S ABSURD UNDER THESE CIRCUMSTANCES; IT'S ALSO UNPRECEDENTED FOR A CBE TO

BE APPROVED UNDER THESE CIRCUMSTANCES.

AND LET ME JUST GO TO ANOTHER PRACTICAL CONSIDERATION. IT GOES TO DR. FLEMING'S ACKNOWLEDGMENT THAT THE DECISION TO PUBLISH IN *THE NEW ENGLAND JOURNAL OF MEDICINE* AND TO DO IT IN CONJUNCTION WITH THE EMA WAS UNPRECEDENTED.

WHY IS THAT IMPORTANT? IT'S IMPORTANT BECAUSE AS HAS BEEN REFLECTED IN COMMENTS IN THE COURTROOM BEFORE, THESE ARE DRUGS THAT ARE WIDELY USED. PANCREATIC CANCER OF SAFETY SIGNAL IS A SERIOUS SAFETY SIGNAL. IT WARRANTED THIS KIND OF SERIOUS INVESTIGATION BY THE FDA. BUT IT ALSO WARRANTED, AT THE END OF THE DAY, A CLEAR STATEMENT, IF ONE COULD BE GIVEN, FOR DOCTORS, ABOUT WHETHER THE WARNING WAS ADEQUATE OR WHETHER THERE WAS A CONCERN THAT REQUIRED A CHANGE.

NOW, REMEMBER HOW THIS STARTS. IT STARTS WITH A DRUG SAFETY COMMUNICATION. AND THE FDA'S FINAL LINE IS WE HAVE NOT REACHED A CONCLUSION ABOUT ANY CAUSAL ASSOCIATION, AND FOR NOW DOCTORS SHOULD CONTINUE TO FOLLOW THE LABELING THAT THEY HAVE.

AND AT THE END OF THE YEAR, THE FDA GOES TO *THE NEW ENGLAND JOURNAL OF MEDICINE*, WE SUBMIT, BECAUSE THEY ARE TRYING TO BRING CLARITY TO DOCTORS ABOUT THESE DRUGS, WHICH ARE WIDELY USED, SO THAT DOCTORS AND PATIENTS, IF IT'S SAFE, CAN CONTINUE TO USE THEM WITH CONFIDENCE.

JUDGE HIGHBERGER: YOU SKIP OVER THE FACT THAT THEY SAY WE HAVE NOT YET REACHED A CONCLUSION. THAT COUNTS FOR NOTHING?

MR. HEARD: WELL, LET ME MAKE TWO DISTINCTIONS IN ANSWERING THAT QUESTION, BECAUSE THE PLAINTIFFS HAVE SAID TWO THINGS, JUDGE HIGHBERGER. ONE, IS THEY HAVE SOMETIMES SAID -- AND I WANT TO MAKE SURE WE ARE KEEPING TWO SEPARATE THINGS APART. THEY HAVE SAID THE FDA DIDN'T COMPLETE ITS INVESTIGATION, THE INVESTIGATION THAT IT PROMISED TO DO IN THE DRUG SAFETY COMMUNICATION.

WELL, THE FDA DID COMPLETE THAT INVESTIGATION BECAUSE IT SAYS SO EXPLICITLY IN THE SECOND PARAGRAPH OF *THE NEW ENGLAND JOURNAL OF MEDICINE* ARTICLE.

HAVE THEY REACHED THE FINAL CONCLUSION, IN THE SENSE THAT COULD NEW SCIENTIFIC EVIDENCE CHANGE THEIR MIND? WELL, YES, I THINK ONE WOULD SAY THEIR CONCLUSIONS COULD CHANGE IN THE FUTURE, BASED ON NEW SCIENTIFIC EVIDENCE, BECAUSE THAT'S TRUE OF ALL DRUGS. THE FDA CONTINUES TO MONITOR, RECOGNIZING THAT NEW SCIENTIFIC EVIDENCE COULD CHANGE THINGS.

NOW, TWO CAVEATS TO THAT. ONE IS THE FDA TELLS US WHAT EVIDENCE IS GOING TO BE SIGNIFICANT TO THEM, WHAT THEY HAVE THEIR EYE ON. AND THEY HAVE THEIR EYE ON THE TWO CLINICAL TRIALS THAT ARE ONGOING, BOTH OF WHICH WERE DISCUSSED IN WEDNESDAY'S HEARING.

SO THEY TOLD US GIVEN THE ENORMOUS AMOUNT OF MATERIAL THAT WE HAVE CONSIDERED, THE KIND OF EVIDENCE THAT COULD NOW BE INFLUENTIAL IS A LARGE-SCALE, RANDOMIZED, DOUBLE-BLIND CLINICAL TRIAL. WITH THAT ADDITIONAL INFORMATION, WE COULD DO THE KIND

OF META-ANALYSIS THAT MIGHT TAKE US TO A DIFFERENT LEVEL IN ASSESSING THE SCIENTIFIC BASIS, NOT JUST ANYTHING.

THE COURT: WE ARE CHECKING YOUR TIME. YOU HAVE 44 MINUTES DOWN. GO AHEAD

MR. HEARD: WELL, I'M GOING TO SPEED UP A LITTLE BIT SO AS NOT TO SHORTCHANGE MR. GOETZ.

THE COURT: SO WE MAKE SURE MR. GOETZ GETS HIS ALLOTMENT. GO AHEAD.

MR. HEARD: AND, OF COURSE, WE'RE CONFRONTED WITH THE ISSUE THAT JUDGE BATTAGLIA MENTIONED ON WEDNESDAY, AND THAT IS THESE ARE DRUGS THAT ARE ON THE MARKET, WE SHOULD EXPECT THEM TO BE CONTINUED TO BE STUDIED, THE SCIENCE ISN'T GOING TO STOP. AND THE LAW, AS ALWAYS, HERE, AS IN THE DAUBERT CONTEXT, HAS GOT TO RESOLVE THE DISPUTES.

SO THE QUESTION ON THE TABLE IS, IS THERE CLEAR EVIDENCE NOW ABOUT WHETHER THE FDA WOULD ADOPT A PANCREATIC CANCER WARNING? AND WE SAY CLEARLY NOT.

NOW, LET ME QUICKLY ADDRESS QUESTION NUMBER FOUR, AND I WILL PASS OVER QUESTION NUMBER FIVE FOR NOW, IN ORDER TO LET MR. GOETZ SPEAK.

THE FOURTH QUESTION IS ABOUT PANCREATITIS AND ITS PRESENCE IN THE LABELING. FIRST OF ALL, OF COURSE, THE PLAINTIFFS ALLEGE THAT THE DRUGS CAUSE PANCREATIC CANCER. SO AT ONE LEVEL HOW THE FDA HAS CHOSEN TO TREAT THE PANCREATITIS IS A DIFFERENT ISSUE. THAT IS NOT OUR ISSUE.

SECONDLY, THE FDA IS ALSO CLEAR ABOUT ITS CONCLUSION ABOUT A PANCREATIC CANCER WARNING; THAT IT'S NOT JUSTIFIED BY THE SCIENCE. SO, AGAIN, WHAT THE FDA HAS DECIDED TO DO ABOUT A PANCREATITIS WARNING IS NOT REALLY AN ISSUE THAT IS RELEVANT NOW.

BUT HAVING SAID THAT, WE KNOW THAT THE FDA LOOKED AT THE VERY TYPE OF EVIDENCE THAT SUPPORTS THE PANCREATITIS WARNING, THE VERY TYPE OF EVIDENCE, AND SAID THAT TYPE OF EVIDENCE IN THE CONTEXT OF PANCREATIC CANCER DOES NOT SUPPORT A PANCREATIC CANTER WARNING.

NOW, TO BE MORE SPECIFIC, WHAT AM I SAYING? WHAT IS THE PANCREATITIS WARNING? IT'S A SIMPLE SENTENCE, VARYING SLIGHTLY FROM LABEL TO LABEL, BUT IT SAYS THERE HAVE BEEN POST-MARKETING REPORTS OF ACUTE PANCREATITIS. PERIOD.

HAS THE FDA LOOKED AT POST-MARKETING REPORTS OF PANCREATIC CANCER? YES, IT HAS.

IT LOOKED AT THEM -- IT LOOKED AT THEM IN REJECTING THE CITIZEN PETITION, AND SAID THAT THE POST-MARKETING REPORTS WERE NO NEW EVIDENCE WARRANTING ANY CHANGE IN THE LABELING.

AND THEY EXPLAINED WHY: PANCREATIC CANCER AND PANCREATITIS ARE DIFFERENT DISEASES, DIFFERENT LATENCY PERIODS, DIFFERENT PROGNOSES, DIFFERENT BACKGROUND RATES IN THE POPULATION.

AND THE FDA'S VIEW, RIGHT OR WRONG, IS THAT POST-MARKETING REPORTS HAVE VERY LITTLE VALUE EVALUATING A

DISEASE THAT IS COMMON IN THE BACKGROUND OF UNTREATED POPULATION, AS PANCREATIC CANCER IS, AND IT HAS A LONG LATENCY PERIOD, AS PANCREATIC CANCER DOES.

SO WE KNOW THE FDA HAS LOOKED AT THE VERY EVIDENCE THAT SUPPORTS THE PANCREATITIS WARNING AND SAID THIS DOESN'T DO IT FOR US FOR PANCREATIC CANCER. IT DOESN'T JUSTIFY A WARNING HERE.

SO WE FIND WHAT IS AN APPARENT INCONSISTENCY, IS NOT. IT'S GROUNDED IN FINDINGS, IT'S GROUNDED IN AN EXPRESSED STATEMENT OF WHY THEY ARE MAKING THE DIFFERENCE. AND SO IT IS NO EVIDENCE THAT BECAUSE THERE IS A PANCREATITIS WARNING THE FDA HAS OPENED THE DOOR TO THE PANCREATIC CANCER WARNING.

SO, YES, THE STANDARD FOR PREEMPTION IS HIGH. IT'S A DEMANDING DEFENSE. BUT THE SUPREME COURT IN *WYETH*, AS IT MIGHT HAVE, DID NOT SHUT THE DOOR, NOR DID IT ESTABLISH A STANDARD THAT WAS IMPOSSIBLE TO MEET. THERE ARE AT LEAST THREE DECISIONS WHICH HAVE FOUND PREEMPTION -- *ROBINSON*, *RECKIS*, *RHEINFRANK*, IN PART, *DOBBS*.

AND THE FACTS HERE, WE SUBMIT, ARE STRONGER THAN IN ANY OF THOSE CASES BECAUSE OF THE UNPRECEDENTED EXERCISE OF EVALUATING THIS FOR A YEAR; AND GIVEN THE WEALTH OF DATA THE FDA TELLS US IT CONSIDERED, ITS CONCLUSION ABOUT THE ADEQUACY TETHERED TO ITS ANALYSIS OF THE SCIENTIFIC EVIDENCE, ITS RETURN TO THE ISSUE IN REJECTING THE CITIZENS' PETITION, ITS RETURN TO THE ISSUE IN THE BRIEFING BOOK, ITS ACTING TO APPROVE LABELING

DURING THIS SAME TIME PERIOD WHEN IT COULD HAVE MANDATED A PANCREATIC CANCER WARNING, BUT DIDN'T.

JUDGE HIGHBERGER: DO WE KNOW HOW MANY TIMES THE FDA HAS HAD ITS SCHOLARS OR A PACK OF SCIENTISTS CONTRIBUTE AN ARTICLE TO *THE NEW ENGLAND JOURNAL OF MEDICINE* OR AN EQUALLY DISTINGUISHED PEER REVIEW JOURNAL?

MR. HEARD: NO. I KNOW ONLY WHAT DR. FLEMING HAS ACKNOWLEDGED, THAT IT'S UNPRECEDENTED.

JUDGE HIGHBERGER: WHICH WOULD SUGGEST IT'S THE FIRST TIME.

MR. HEARD: WHICH WOULD SUGGEST IT'S THE FIRST OR ONLY TIME.

JUDGE HIGHBERGER: BUT FLEMING CONCEDED AS MUCH?

MR. HEARD: HE DID.

JUDGE HIGHBERGER: AND DO WE KNOW HOW MANY TIMES THE FDA HAS ENGAGED IN THE JOINT SCIENTIFIC REVIEW WITH THE EUROPEAN MEDICAL SAFETY BUREAUCRATS?

MR. HEARD: MY ANSWER WOULD BE THE SAME.

I AM GOING TO DEFER TO MR. GOETZ. THANK YOU, YOUR HONORS.

THE COURT: MR. GOETZ.

MR. GOETZ: I WOULD LIKE TO ADDRESS TWO OR THREE QUESTIONS, PARTLY ADDRESSED TO THE STANDARD THAT THIS COURT IS SUPPOSED TO APPLY, AND THAT JUDGE HIGHBERGER HAS RAISED IN HIS TENTATIVE OPINION: WHAT DOES IT MEAN TO FIND CLEAR EVIDENCE?

AND I THINK THE MOST IMPORTANT FRAMING OF THAT ISSUE IS WHAT'S THERE SUPPOSED TO BE CLEAR EVIDENCE OF? AND HERE IT'S HAS THE FDA CONCLUDED THAT THE SCIENCE DOES NOT SUPPORT ADDING CANCER TO THE LABEL.

THE FDA IS A SCIENCE-BASED AGENCY. AND WE'VE SEEN FROM MR. HEARD THE MULTIPLE STATEMENTS BY THE FDA IN ITS OWN REGULATORY SCHEME ON THAT QUESTION, THAT THE FDA HAS CONCLUDED THAT THE CURRENT SCIENCE DOES NOT SUPPORT ADDING CANCER TO THE LABEL.

(PHONE DISRUPTION/MUSIC PLAYING)

THE COURT: THAT'S COMING FROM THE PHONE?

MR. GOETZ: I THINK THAT'S COMING FROM THE PHONE, YOUR HONOR.

THE COURT: TURN OFF YOUR MUZAK, WHOEVER HAS THAT, OR WE WILL HAVE TO CUT OFF THE PHONE.

(PAUSE IN PROCEEDINGS)

MR. GOETZ: SHALL I PROCEED?

THE COURT: WHILE WE RESOLVE THIS -- IT SOUNDS LIKE THEY HAVE GOT IT. GO AHEAD.

MR. GOETZ: THANK YOU. AND IN ADDRESSING THE CLEAR EVIDENCE STANDARD, I THINK --

(PHONE DISRUPTION/MUSIC PLAYING)

THE COURT: WE ARE GOING TO CUT OFF THE PHONE AND LET MR. GOETZ HAVE THE COURTESY OF NO DISTRACTION. SO WE ARE GOING TO HANG UP ON THE FOLKS ON THE PHONE.

JUDGE HIGHBERGER: I CONCUR.

(TELEPHONIC HEARING SUSPENDED)

THE COURT: OKAY. GO AHEAD, MR. GOETZ. I BELIEVE THAT WILL BE ON THE RECORD.

MR. GOETZ: I USUALLY DO THIS TO MUSIC, YOUR HONOR, SO THANK YOU.

THE OTHER IMPORTANT THING I WANT TO SET FORTH -- AND THIS IS, AGAIN, ADDRESSED TO JUDGE HIGHBERGER'S QUESTION AND STATEMENT IN HIS TENTATIVE: WHAT DOES IT MEAN TO HAVE CLEAR EVIDENCE, AND WHY DID *WYETH* PICK A CLEAR EVIDENCE STANDARD RATHER THAN IRONCLAD EVIDENCE, UNDISPUTED EVIDENCE, 100 PERCENT CERTAINTY?

I THINK THE ANSWER TO THAT QUESTION IS WE WILL NEVER KNOW FOR CERTAIN EVERYTHING THAT GOES ON IN A FEDERAL AGENCY, SUCH AS THE FDA.

THE SUPREME COURT ACKNOWLEDGED THAT WHEN IT SET FORTH A STANDARD THAT DIDN'T REQUIRE IRONCLAD EVIDENCE, DIDN'T REQUIRE IT BE, IN A SUMMARY JUDGMENT STANDARD, AN UNDISPUTED FACT WHAT THE FDA WOULD DO. THAT IS NOT THE STANDARD THAT THE UNITED STATES SUPREME COURT PUT FORTH.

AND WHY IS THAT? IT'S BECAUSE, I THINK, IN MOST CASES WHEN YOU ARE ASKED TO RULE ON A SUMMARY JUDGMENT MOTION, FOR EXAMPLE, YOU HAVE, ESSENTIALLY, TWO PARTIES BEFORE YOU. AND YOU ARE ASKED TO TAKE AWAY FROM THE JURY SOMETHING THAT WOULD NORMALLY BELONG TO THE JURY AS A QUESTION. AND YOU TREAD

LIGHTLY WHEN YOU DO THAT BECAUSE YOU ARE INTERFERING WITH THE APPROPRIATE PROCESS OF THE COURTS.

THIS IS VERY DIFFERENT. HERE YOU ARE BEING ASKED AS OFFICERS OF THE COURT, WHAT WOULD THE FDA HAVE DONE HERE, WHAT WAS THE FDA'S SCIENCE CONCLUSION? BECAUSE THE FDA IS CHARGED WITH PROTECTING A LOT OF PEOPLE WHO AREN'T IN THIS COURTROOM.

JUDGE HIGHBERGER: YOU ARE CONTENDING THAT'S A QUESTION OF LAW, NOT A QUESTION OF FACT?

MR. GOETZ: IT IS A QUESTION OF LAW, YOUR HONOR. IT IS A QUESTION THAT YOU MUST ANSWER. AND THE QUESTION IS, UNDER *WYETH*, HAVE WE PRESENTED CLEAR EVIDENCE THAT THE FDA HAS MADE THIS SCIENTIFIC CONCLUSION. IT DOESN'T NEED TO BE EVEN UNDISPUTED EVIDENCE. IT NEEDS ONLY BE CLEAR.

AND THAT IS BECAUSE THE SUPREME COURT IS ACKNOWLEDGING THE IMPORTANCE OF TAKING INTO ACCOUNT THE INTERESTS OF THE FDA, AND THE INTERESTS OF THE PEOPLE NOT BEFORE THE COURT.

THE CALIFORNIA SUPREME COURT HAS HELD THE SAME THING, YOUR HONOR, IN A CASE THAT I KNOW YOU ARE FAMILIAR WITH, THE *DOWHAL V. SMITHKLINE BEEHAM AND CONSUMER HEALTHCARE* CASE, AT 32 CAL.4TH 910, IN 2004.

NOW, THAT WAS A PROP. 65 CASE, BUT HERE IS WHAT THE CALIFORNIA SUPREME COURT SAID, MUCH ON THE SAME POLICY GROUNDS AS WE SAW IN *WYETH*: AS WE HAVE NOTED, A TRUTHFUL WARNING OF AN UNCERTAIN OR REMOTE DANGER MAY MISLEAD THE CONSUMER INTO

MISJUDGING THE DANGER STEMMING FROM THE USE OF A PRODUCT AND CONSEQUENTLY MAKING A MEDICALLY UNWISE DECISION. THE AUTHORITY OF THE FDA, WE CONCLUDE, EXTENDS TO BARRING WARNINGS THAT ARE MISLEADING IN THIS FASHION.

SO THAT IS WHY THIS IS A QUESTION OF LAW. BOTH THE CALIFORNIA SUPREME COURT AND THE UNITED STATES SUPREME COURT HAVE ACKNOWLEDGED THE IMPORTANCE OF GETTING THIS RIGHT, AND OF PROTECTING THE INTEREST OF PEOPLE NOT JUST IN THE COURTROOM, BUT THE PEOPLE WHO WILL BE READING THIS LABEL AND MAY BE MISLED BY ADDING TO THE LABEL SOMETHING THAT THE FDA HAS CONCLUDED IS UNWARRANTED UNDER THE SCIENCE.

LOOKING BACK, YOUR HONOR HAS ASKED THE QUESTION HOW CAN WE KNOW WHAT WAS IN THE FDA'S MIND PRIOR TO THE NEJM STATEMENT, *THE NEW ENGLAND JOURNAL OF MEDICINE* ARTICLE, THE EGAN ARTICLE IN 2014. AND I WOULD SUBMIT THAT THE RECORD HERE IS CLEAR THAT EVERY DAY BEFORE THAT ARTICLE THE SCIENCE WAS EVEN WEAKER. IT'S NOT LIKE THE SCIENCE WAS STRONG IN 2011 AND SOMETHING HAPPENED TO CHANGE THE SCIENCE IN 2014 THAT CAUSED THE FDA TO COME OUT WITH ITS ARTICLE.

SO WHEN THE FACTUAL QUESTION, THAT TURNS INTO A LEGAL QUESTION WHEN PRESENTED TO YOUR HONOR, OF "HAS THE FDA CONCLUDED SCIENCE DOES NOT SUPPORT ADDING CANCER TO THE LABEL" IS ASKED IN ANY PRIOR PERIOD, PLAINLY THE SCIENCE WOULD EVEN BE WEAKER TO ADD IT TO THE LABEL.

BUT THERE IS ANOTHER REASON -- CONFLICT PREEMPTION --

WHY I SUBMIT, AS A LEGAL MATTER, YOU SHOULD NOT HAVE A LABEL IN 2011 -- ORDER A CASE THAT COULD GO FORWARD BASED ON A 2011 FACT-PATTERN, GIVEN WHAT HAS HAPPENED IN 2014 IN *THE NEW ENGLAND JOURNAL* ARTICLE.

AND THAT GOES BACK TO THE *DOWHAL* CASE. AND IT GOES BACK TO A LONG LINE OF CONFLICT PREEMPTION CASES. UNITED STATES SUPREME COURT, FOR EXAMPLE, IN *CROBSY V. NATIONAL FOREIGN TRADE ASSOCIATION COUNCIL,* 530 U.S. 363. THEY ARE DEALING WITH MASSACHUSETTS ATTEMPTING TO GOVERN RELATIONS WITH MYANMAR, MUCH AS THE FEDERAL GOVERNMENT WAS ALSO TRYING TO REGULATE THEM.

AND HERE IS WHAT THE CONFLICT PREEMPTION IS. YOU HAVE THE FDA TAKING AN UNPRECEDENTED STEP IN *THE NEW ENGLAND JOURNAL OF MEDICINE*, SENDING A MESSAGE CLEARLY TO THE PRESCRIBING COMMUNITY. NOW, THEY COULD HAVE JUST WRITTEN US LETTERS, BUT THEY REACHED OUT TO THE PRESCRIBING COMMUNITY BECAUSE THEY WANTED THE PRESCRIBING COMMUNITY TO UNDERSTAND THAT THEY HAD COME TO THE CONCLUSION -- SUBJECT TO REVISITING, BUT AS OF THAT ARTICLE -- THEY HAVE COME TO THE CONCLUSION THAT THE SCIENCE DOES NOT SUPPORT ADDING CANCER TO THE LABEL.

IF YOU ALLOW LAWSUITS TO GO FORWARD FROM 2011, 2010, 2013, THE DAY BEFORE *THE NEW ENGLAND JOURNAL* ARTICLE, ANY OF THOSE PERIODS, YOU UNDERMINE THOSE EFFORTS OF THE FDA. YOU UNDERMINE THE CLEAR MESSAGE, THE UNPRECEDENTED MESSAGE IT WENT TO GREAT LENGTHS TO SEND OUT TO THE PRESCRIBING PUBLIC.

SO THAT IS AN INDEPENDENT REASON, IN ADDITION TO IMPOSSIBILITY PREEMPTION, WHY YOU WOULD NOT LOOK TO EARLIER DATES AND COME TO A DIFFERENT CONCLUSION ON THE LABELING OF THESE PRODUCTS.

I WOULD SAY IF YOU LOOK BACK AT WHAT WAS IN THE RECORD, YOU HAD NOT JUST *THE NEW ENGLAND JOURNAL* ARTICLE COME OUT OF THE BLUE; YOU HAD THE VICTOZA APPROVAL IN 2010, THE TRAJENTA APPROVAL 2011, THE REVIEW OF THE VICTOZA LABEL BY THE CITIZEN'S PETITION IN 2014, BYDUREON APPROVAL IN 2012, AND SO ON. AND THE EMA ASSESSMENT THAT WE TALKED ABOUT AT SCIENCE DAY IN 2013.

AND ONE OTHER QUESTION I WANT TO ANSWER TO YOUR HONOR, JUDGE HIGHBERGER, YOU ASKED IS *DOBBS* ALONE. WE ALREADY HEARD FROM MR. HEARD IS *DOBBS* ALONE. BUT WE KNOW ALSO FROM THE BRIEFING THAT YOU ALREADY HAVE THAT IN THE *FOSAMAX* CASE, IN THE DISTRICT COURT OF NEW JERSEY IN 2013, THE FDA EXPRESSLY REJECTED PROPOSED LABEL CHANGES.

SO IT'S NOT THE CASE THAT THE FDA WILL ALWAYS ACCEPT ANY PROPOSED LABELING CHANGES SUBMITTED BY A COMPANY. AND, INDEED, IT MAKES NO SENSE TO BELIEVE THEY WOULD DO SO HERE.

JUDGE HIGHBERGER: WHAT IS THE CITE TO THAT NEW JERSEY CASE?

MR. GOETZ: I WILL GET THAT FOR YOU, YOUR HONOR.

JUDGE HIGHBERGER: YOU CAN FURNISH IT AFTER THE HEARING.

MR. GOETZ: WE WILL.

NOW, IN THE MANY, MANY MINUTES I HAVE LEFT, WE DID SKIP OVER ISSUE FIVE. IT'S AN IMPORTANT ISSUE. THAT IS THE QUESTION OF WHAT ABOUT THE ARGUMENTS THAT CAN ALWAYS BE MADE ON ANY LABEL AT ANY TIME, THAT THERE IS MORE YOU COULD HAVE GIVEN TO THE FDA. AND I SUSPECT IN THE NEXT HOUR YOU ARE GOING TO HEAR A GREAT DEAL FROM THE PLAINTIFFS ON EXACTLY THAT POINT.

I WOULD SUBMIT A FEW THINGS ON THAT, AND I'M SURE WE WILL REVISIT THIS ISSUE IN REBUTTAL. ONE IS THE PLAINTIFFS HAVE OFFERED NO EXPERT TESTIMONY, DESPITE GIVEN THE TIME TO DO SO, THAT ANY OF THOSE DATA POINTS WOULD MATTER TO THE FDA.

THE SECOND IS WHAT JUDGE BATTAGLIA HAS SAID IN THE PAST, ABOUT THE EXTENT OF *BUCKMAN*, THAT THIS IS, IN ESSENCE, A FRAUD ON THE FDA CLAIM. BUT IT'S A FRAUD ON THE FDA CLAIM IN A VERY UNUSUAL AND DANGEROUS WAY.

IT'S THAT THE LABEL OR THE DECISION OF THE FDA, ITS SCIENTIFIC CONCLUSIONS CAN BE DISREGARDED BECAUSE OF AN ALLEGED FRAUD ON THE FDA. I KNOW OF NO WAY TO DRAW A LIMIT AROUND THAT. I KNOW OF NO ACTUAL LABEL WHERE YOU COULDN'T SAY THE LABEL IS WRONG BECAUSE THE FDA DIDN'T HAVE ENOUGH INFORMATION. NO SCIENTIFIC CONCLUSION THAT THE FDA COULD COME TO WHERE YOU COULDN'T MAKE THE ARGUMENT THAT THE FDA GOT IT WRONG BECAUSE IT DIDN'T HAVE EVERYTHING THAT WE THINK IT SHOULD HAVE HAD BEFORE IT.

AND LOOK AT THE EXTENT THAT YOU WILL HEAR FROM THE

PLAINTIFFS, I SUSPECT, ON WHAT WE SHOULD HAVE GIVEN.

JUDGE HIGHBERGER, YOU ARE QUITE FAMILIAR WITH THE CLIVE TAYLOR REPORT. YOU SAW THAT IN THE PANCREATITIS CASES, AND YOU ORDERED THAT DR. TAYLOR COULD NOT TESTIFY ABOUT PANCREATIC CANCER. IN PART, YOU DID THAT, I BELIEVE, BECAUSE IN THE 402 HEARING BEFORE JUDGE WEST -- AND WE GAVE YOU THAT RECORD -- WHEN I CROSS-EXAMINED DR. TAYLOR, HE HAD ADMITTED THAT HE SAW NO EVIDENCE IN ANY OF THOSE SLIDES OF PANCREATIC CANCER, AND HE WAS NOT THERE TO TESTIFY THAT HE FOUND PANCREATIC CANCER.

SO THERE IS A LOT OF STRETCH HERE ON WHAT YOU ARE GOING TO HEAR ABOUT BEING GIVEN TO THE FDA AND HOW IT WOULD HAVE MATTERED.

BUT I COME BACK TO THE LEGAL QUESTION: IT DOESN'T MATTER WHETHER YOU BELIEVE THAT EVIDENCE IS STRONG OR NOT. THE FDA IS COMPETENT TO POLICE ITS OWN DOCKET. THAT IS WHAT THE *BUCKMAN* CASE SAYS. AND WE SUBMIT THAT THE FDA'S CONCLUSION ON THE SCIENTIFIC EVIDENCE HERE COULD NOT BE CLEARER.

WHEN I STOOD UP AND I SAID YOU DON'T NEED AN IRONCLAD PIECE OF EVIDENCE HERE ON WHAT THE FDA'S SCIENTIFIC CONCLUSION WAS, I ACTUALLY THINK WE DO. WE HAVE THE FDA, AS YOU SAW MR. HEARD START WITH, SAY EXACTLY THAT. WE DO NOT BELIEVE THAT THE SCIENCE SUPPORTS A CONCLUSION OF CAUSATION.

AND YOU HEARD FROM DR. FLEMING, AGREEING THAT THAT WAS THE FDA'S VIEWS. PLAINLY, IT'S CLEAR EVIDENCE. BUT I

WOULD SUBMIT ON THIS QUESTION FIVE, AND I KNOW WE WILL RETURN TO THIS, THAT THERE IS NOTHING THAT YOU WILL HEAR FROM THE PLAINTIFFS -- YOU'VE HEARD IT ALL BEFORE -- THAT AS A FACTUAL MATTER WOULD CAUSE YOU TO CONCLUDE THAT THE FDA WOULD MAKE A DIFFERENT CONCLUSION. BUT, MORE IMPORTANTLY, AS A LEGAL MATTER, THAT YOU COULD MAKE THAT CONCLUSION.

THE COURT: WELL, THANK YOU. YOUR TIME IS COMPLETE, UNLESS YOU WANT TO FURNISH THAT CITE THAT WAS JUST HANDED TO YOU.

MR. GOETZ: I DO HAVE THE CITE. IT'S 951 F. SUPP. 2D 695.

THE COURT: SO WE'LL TAKE A SECOND. WHAT IS THE PAGE NUMBER? I STARTED TO TALK WHILE I WAS WRITING, AND I FORGOT WHAT YOU SAID.

MR. GOETZ: I'M SORRY. 951 F. SUPP. 2D 695.

THE COURT: CAN YOU NAME THE PARTIES?

MR. GOETZ: IT'S *IN RE: FOSAMAX PRODUCT LIABILITY LITIGATION.*

THE COURT: THANK YOU.

ALL RIGHT. WE'LL TAKE A TEN-MINUTE BREAK AND THEN CONTINUE WITH THE PRESENTATION.

(RECESS FROM 10:07 A.M. TO 10:20 A.M.)

(RESUMING TELEPHONIC CONNECTION)

THE COURT: WE ARE BACK IN JOINT SESSION, AND IT'S NOW TIME FOR THE PLAINTIFFS' TURN.

AND WHO IS GOING TO BE PROCEEDING FIRST ON BEHALF OF THE PLAINITIFFS?

MR. BOGRAD: I WILL BE, YOUR HONOR. LOUIS BOGRAD FROM THE CENTER FOR CONSTITUTIONAL LITIGATION.

THE COURT: OKAY. MR. BOGRAD, WHEN READY, YOU MAY PROCEED.

MR. BOGRAD: MAY I HAVE JUST ONE MORE MOMENT, YOUR HONOR?

THE COURT: YES. TELL US WHEN YOU ARE READY TO GO.

(PAUSE)

WHILE YOU ARE GETTING READY, I JUST MENTIONED WE HAVE REESTABLISHED THOSE ON THE PHONE, WITH THE EXCEPTION OF THE OFFENDING PARTY, SO THEY ARE BACK WITH US. FEEL FREE TO PROCEED, SIR.

MR. BOGRAD: MAY IT PLEASE THE COURT, LOUIS BOGRAD FOR THE MDL PLAINTIFFS.

UNLIKE DEFENDANTS, WE ARE GOING TO PROCEED IN A SLIGHTLY DIFFERENT MANNER, YOUR HONOR.

THE COURT: OKAY.

MR. BOGRAD: MY LEAD COUNSEL FROM THE JCCP, MS. CROOKE AND MR. DEPEW, HAVE INVITED ME TO TAKE THE LEAD ON THIS ARGUMENT, SO I WILL BE COVERING THE WATERFRONT, SO TO SPEAK.

I KNOW YOU ARE VERY FAMILIAR WITH MR. KENNERLY. HE HAS A BETTER HANDLE ON SOME OF THE SCIENCE THAN I DO. SO IF WE

FIND OURSELVES WITH A QUESTION THAT I FEEL INCAPABLE TO ANSWER, I MAY TURN TO HIM FOR HELP.

AND MS. CROOKE AND MR. DEPEW WILL COME UP AT THE END, IF THEY ARE INCLINED TO DO SO, TO FILL IN ANYTHING THEY FEEL THAT I HAVE LEFT OUT, CORRECT ANY MISTAKES I HAVE MADE, OR ANSWER ANY QUESTIONS THAT ARE SPECIFIC TO THE JCCP.

BEFORE I TURN TO THE SUBSTANCE OF MY ARGUMENT, I THINK IT'S IMPORTANT TO RESPOND TO TWO THINGS YOU JUST HEARD FROM MR. GOETZ, BECAUSE I THINK THEY ARE COMPLETELY MISLEADING AND INACCURATE.

FIRST, THERE WAS THE SUGGESTION FROM THE *DOWHAL* CASE THAT THE FDA HAS THE AUTHORITY TO PROHIBIT MISLEADING WARNINGS. WE DO NOT DISAGREE. PLAINTIFFS HAVE NEVER CONTENDED THAT WHAT WE ARE AFTER HERE IS A MISLEADING WARNING ABOUT THE RISK OF PANCREATIC CANCER. THE QUESTION IS WHETHER THERE SHOULD HAVE BEEN AN ACCURATE, TRUTHFUL AND NOT MISLEADING WARNING ABOUT PANCREATIC CANCER. AND THAT'S THE ONLY ISSUE BEFORE THE COURT. NO ONE IS CONTENDING A WARNING THAT WAS NOT SCIENTIFICALLY JUSTIFIED SHOULD HAVE BEEN ADDED TO THE LABEL.

SECONDLY, I THINK IT'S IMPORTANT TO FOCUS ON ANOTHER POINT THAT MR. GOETZ MADE ABOUT THE SUPREME COURT'S DECISION IN *WYETH V. LEVINE* THAT MISSTATES, TO MY MIND, COMPLETELY, THE REASON WHY WE HAVE THIS CLEAR EVIDENCE EXCEPTION TO THE HOLDING IN THAT CASE.

HE SAID THIS IS OUT OF RESPECT FOR THE FDA AND TO

PROTECT THE FDA'S INTERESTS. FRANKLY, THAT HAS NOTHING TO DO WITH IT. AS THE SUPREME COURT SAID IN THAT DECISION, STATE TORT LAW COMPLIMENTS THE FEDERAL REGULATORY SYSTEM. IT NOT ONLY PROVIDES ACCESS TO INFORMATION THAT MIGHT NOT OTHERWISE EXIST; IT CREATES INCENTIVES FOR MANUFACTURERS TO BRING INFORMATION TO THE FDA THAT THEY MIGHT OTHERWISE CHOOSE TO WITHHOLD, AND IT PROVIDES AN IMPORTANT COMPENSATORY FUNCTION.

SO THEY CERTAINLY DIDN'T SAY THAT WE'RE GOING TO CREATE A BASIS FOR PRESUMPTION IN ORDER TO PROTECT THE FDA. STATE TORT LAW PROTECTS THE FDA, IN THE SUPREME COURT'S VIEW.

WHAT THEY SAID IS THAT UNDER THE DOCTRINE OF IMPOSSIBILITY PREEMPTION, THAT THERE MAY BE SOME VERY LIMITED CIRCUMSTANCES IN WHICH IT WOULD BE IMPOSSIBLE FOR A DEFENDANT TO DO THAT WHICH THE STATE -- THE PLAINTIFFS ARE SAYING STATE LAW REQUIRED THEM TO DO.

THAT WAS THE ISSUE IN *MENSING*, WHERE THE SUPREME COURT SAID IT WOULD BE IMPOSSIBLE FOR A GENERIC DRUG COMPANY TO CHANGE ITS LABEL BECAUSE FEDERAL LAW REQUIRED IT TO BE THE SAME.

AND WHAT THE SUPREME COURT SAID IN *WYETH V. LEVINE* IS THAT EVEN THOUGH IN THE VAST MAJORITY OF CASES THERE IS NO PREEMPTION BECAUSE A DRUG COMPANY IS ALWAYS FREE TO USE THE CBE PROCESS TO ADD A NEW WARNING WHEN IT BELIEVES THAT THERE IS SCIENCE THAT SUPPORTS THAT WARNING, THERE MIGHT BE SOME VERY RARE CIRCUMSTANCES IN WHICH ACTIONS TAKEN BY THE FDA PROVIDE

CLEAR EVIDENCE THAT THE FDA WOULD HAVE PROHIBITED THEM FROM ADDING THAT WARNING. AND IN THAT NARROW CIRCUMSTANCE, WE MIGHT HAVE AN ACTUAL SITUATION OF IMPOSSIBILITY.

SO I THINK IT'S IMPORTANT THAT WE CLEAR THE AIR ON THAT POINT. THE ISSUE HERE IS IMPOSSIBILITY. AND IT'S IMPOSSIBILITY BECAUSE OF THE SUPREMACY CLAUSE AND THE TENSION BETWEEN FEDERAL AND STATE LAW THAT MAY OR MAY NOT EXIST. IT'S NOT ABOUT PROTECTING THE FDA OR RESPECTING ITS JUDGMENTS ABOUT THE RIGHTNESS OR WRONGNESS, BECAUSE THE COURT IS VERY CLEAR THAT WHAT WE ARE ALL DOING HERE IS BENEFICIAL TO THE REGULATORY PROCESS.

WITH THAT, LET ME TURN AND FOCUS MY ARGUMENT. AS THE SUPREME COURT SAID IN *WYETH*, IMPOSSIBILITY PREEMPTION IS A DEMANDING DEFENSE. DEFENDANTS MUST SHOW, BY CLEAR EVIDENCE, THAT THE FDA WOULD NOT HAVE APPROVED A LABEL CHANGE IF THE DEFENDANTS HAD PROPOSED ONE. OR, TO PUT IT MORE FORCEFULLY, AS THE SUPREME COURT DID TWO YEARS LATER IN THE *MENSING* CASE, IN ORDER TO ESTABLISH A PREEMPTION, DEFENDANTS MUST PROVE BY CLEAR EVIDENCE THAT THE FDA WOULD HAVE RESCINDED ANY CHANGE IN THE LABEL THAT DEFENDANTS HAD MADE THROUGH CBE. THAT IS THE *MENSING* DECISION AT 131 S. COURT 2581, NOTE 8.

THE DEFENDANTS' BURDEN ON THIS MOTION IS EXTREMELY HIGH. IN AN EARLIER PRESUMPTION CASE, *RICE V. NORMAN WILLIAMS*, THE SUPREME COURT SAID THAT ONLY A REAL CONFLICT BETWEEN STATE AND FEDERAL LAW WILL JUSTIFY PREEMPTION. A HYPOTHETICAL OR

POTENTIAL CONFLICT IS INSUFFICIENT TO WARRANT PREEMPTION.

AND AT THEIR CORE, DEFENDANTS' ENTIRE MOTION IS BASED ON JUST SUCH A HYPOTHETICAL CONFLICT, ON SPECULATION ABOUT WHAT THE FDA WOULD HAVE DONE IF THEY HAD EVER ACTUALLY SUBMITTED A CBE CONCERNING PANCREATIC CANCER.

ALL OF THE DEFENDANTS' PROOF THAT THEY PUT BEFORE YOUR HONORS SPEAKS TO THE QUESTION WHETHER FDA THOUGHT THERE WAS SUFFICIENT EVIDENCE FOR A WARNING TO BE REQUIRED, NOT WHETHER ONE WOULD BE PERMITTED.

TO QUOTE *LEVINE*, AGAIN, THE VERY IDEA THAT THE FDA WOULD BRING AN ENFORCEMENT ACTION AGAIN A MANUFACTURER FOR STRENGTHENING A WARNING THROUGH CBE IS DIFFICULT TO ACCEPT. NEITHER *WYETH* OR THE UNITED STATES HAS IDENTIFIED A CASE WHERE THE FDA HAS DONE SO.

FOR THIS REASON, CASES OF CLEAR EVIDENCE ARE EXCEEDINGLY RARE. AND IN EACH OF THE CASES WHERE CLEAR EVIDENCE HAS BEEN FOUND, THE MANUFACTURER ACTUALLY PROPOSED A WARNING WHICH WAS REJECTED BY THE FDA -- THAT WOULD BE THE *DOBBS* CASE, THE *FOSAMAX* CASE, AND THE *RHEINFRANK* CASE THAT WAS JUST MENTIONED.

OR, THE FDA ORDERED THE MANUFACTURER NOT TO ADD A WARNING. *DOBBS*, AGAIN. OR, THE FDA ORDERED THE MANUFACTURER TO ADD LANGUAGE TO THEIR LABEL THAT WAS DIRECTLY CONTRARY TO THE PROPOSITION THAT PLAINTIFFS WERE ASSERTING.

IN THE *DOBBS* CASE, THE FDA ORDERED THE MANUFACTURER

TO PUT A STATEMENT ON THEIR WARNING ABOUT THE RISK OF SUICIDALITY IN ADOLESCENTS WHO USE -- I'VE FORGOTTEN WHICH SSRI DRUG. THEY REQUIRED THEM TO ADD A STATEMENT THAT SAID THERE IS NO EVIDENCE OF AN INCREASED RISK OF SUICIDALITY IN ADULTS.

WE HAVE NOTHING LIKE THAT HERE. NONE OF THE DEFENDANTS EVER SOUGHT FDA PERMISSION TO ADD AN ADVERSE REACTION OR WARNING ABOUT PANCREATIC CANCER.

NONE OF THEM HAVE EVEN GONE TO THE FDA AND SOUGHT ADVICE ABOUT WHAT THEY SHOULD DO ABOUT PANCREATIC CANCER. INSTEAD, THEY ASK YOUR HONORS TO SPECULATE HOW THE FDA WOULD HAVE RESPONDED TO A PROPERLY SUPPORTED CBE.

THE COURT: BUT WHY WOULD THEY GO WITH A CBE IF THEY FEEL THEY HAVE NO EVIDENCE OF A CAUSAL CONNECTION SUFFICIENTLY ESTABLISHED OR REASONABLY ESTABLISHED? I MEAN, WHY WOULD THEY?

MR. BOGRAD: YOUR HONOR, IF THEY WERE RIGHT, IF THAT'S THEIR JUDGMENT AND IF THAT JUDGMENT IS CORRECT, THEN THEY WOULD WIN THIS CASE ON CAUSATION. BECAUSE THEN WE WOULD GO TO CAUSATION, THE COURT WOULD LOOK AT THE EVIDENCE AND SAY WELL, I'VE WEIGHED ALL THE SCIENCE, THE EXPERTS HAVE TOLD ME WHAT THEY THINK ABOUT THE SCIENCE, AND THEY WIN.

BUT THEY DON'T GET PREEMPTION JUST BECAUSE -- YOU KNOW, NOW, YES, MAYBE SOME DEFENDANT WILL GO FILE -- SOME DRUG COMPANY WILL FILE A CBE THAT THEY DON'T THINK IS JUSTIFIED -- THOUGH, AS THEY SAY THAT WOULD BE A VIOLATION OF LAW IN ORDER TO TRY TO GIN-UP A PREEMPTION DEFENSE. BUT WHY DO THEY NEED TO

IF THE SCIENCE IS SO CONVINCING THAT THEY DON'T HAVE THE BASIS TO ADD THE WARNING IN THE FIRST PLACE?

BUT TO GET AROUND THIS PROBLEM THAT THEY'VE NEVER ASKED FOR A CBE, THE DEFENDANTS' BRIEFING DOES SOMETHING EXTRAORDINARY. THEY ARGUE THAT *WYETH V. LEVINE* IS NO LONGER THE LAW.

THIS IS AT THE DEFENDANTS' REPLY BRIEF IN SUPPORT OF THEIR SUMMARY JUDGMENT MOTION, AT PAGES THREE AND FOUR.

THEY CONTEND -- WITHOUT, I MIGHT ADD, A SINGLE CITATION TO AUTHORITY -- THAT A 2007 AMENDMENT TO THE FDCA TO STRENGTHEN THE FDA'S ABILITY TO COMPEL LABELING CHANGES, QUOTE, CHANGES THE CLEAR EVIDENCE ANALYSIS.

WHEREAS BEFORE 2007, THEY SAY, THE MANUFACTURER HAD THE PRIMARY RESPONSIBILITY FOR ENSURING THE ADEQUACY OF ITS LABELING -- WHICH IS WHAT *WYETH* SAID. NOW THAT RESPONSIBILITY, THEY CONTEND, FALLS TO THE FDA: AFTER 2007, FDA'S FAILURE TO MANDATE A NEW WARNING PROVES THE DEFENDANTS HAD NO BASIS EVEN TO PROPOSE ONE BY CBE. THAT'S THEIR ARGUMENT.

WELL, THAT ARGUMENT WOULD CERTAINLY COME AS A SURPRISE TO THE UNITED STATES SUPREME COURT, WHICH TOOK NOTE OF THE 2007 STATUTORY AMENDMENT IN *LEVINE*, YET NEVER SUGGESTED ITS HOLDING WAS LIMITED TO PRE-2007 CASES.

INSTEAD, THE COURT EXPRESSLY OBSERVED THAT WHEN CONGRESS ENACTED THIS STATUTORY CHANGE, IT ALSO ADOPTED A RULE OF CONSTRUCTION TO MAKE IT CLEAR THAT EVEN WITH THIS ENHANCED

FDA AUTHORITY, THE MANUFACTURER REMAINED RESPONSIBLE FOR UPDATING THEIR LABELS, REMAINED RESPONSIBLE FOR COMPLYING WITH BOTH 201.57 AND WITH 314.70, THE PROVISIONS THAT ALLOW FOR SUPPLEMENTATION.

AND IT WOULD ALSO SUPPRESS THE MANY COURTS THAT HAVE HELD, BOTH BEFORE AND AFTER *LEVINE*, THAT THE FDA'S FAILURE TO MANDATE A WARNING DOES NOT CONSTITUTE CLEAR EVIDENCE THAT THE AGENCY WOULD HAVE REJECTED ONE HAD THE MANUFACTURER PROPOSED IT.

AND IN THAT REGARD, THERE IS THE *MASON* CASE FROM THE SEVENTH CIRCUIT, THE *DORSETT* AND *MOTUS* CASES FROM THE CENTRAL DISTRICT OF CALIFORNIA AND OTHERS, ALL OF WHICH WE'VE CITED IN OUR BRIEFS.

BUT THAT IS REALLY DEFENDANTS' ARGUMENT HERE, THAT BECAUSE THE FDA HAS NOT MANDATED A PANCREATIC CANCER WARNING WE HAVE CLEAR EVIDENCE THAT THEY WOULDN'T HAVE PERMITTED ONE. AND THAT, AS A MATTER OF LOGIC, DOES NOT FOLLOW, AS A MATTER OF FACT DOES NOT FOLLOW.

THERE ARE SEVERAL CRITICAL FLAWS IN DEFENDANTS' ARGUMENT. FIRST, THEY ESSENTIALLY PRESUME THAT THERE IS SOME MAGIC QUANTUM OF EVIDENCE THAT DEFINES REASONABLE EVIDENCE OF A CAUSAL RELATIONSHIP BETWEEN THE DRUG AND THE OCCURRENCE OF THE ADVERSE EVENT, WHICH IS THE STANDARD FOR ADDING A WARNING UNDER 201.57(C)(6), AS WELL AS SOME FIXED QUANTUM OF EVIDENCE THAT WOULD CONSTITUTE SOME BASIS TO BELIEVE THERE IS A CAUSAL

RELATIONSHIP, THE STANDARD FOR ADDING AN ADVERSE EVENT.

THERE ISN'T, AS THE AGENCY ITSELF HAS TOLD US -- AND THIS IS AT 73 FEDERAL REGISTER 49603 -- THAT REGULATORY LANGUAGE IS NOT MEANT TO SUGGEST THAT THERE IS A MATHEMATICALLY PRECISE DISTINCTION BETWEEN WHETHER THERE IS OR IS NOT SUFFICIENT EVIDENCE OF A CAUSAL RELATIONSHIP BETWEEN A DRUG AND AN ADVERSE EVENT TO SUPPORT ITS INCLUSION IN LABELING.

AND FURTHER, IN THE SAME FEDERAL REGISTER NOTICE, THEY SAY CAUSATION NEED NOT HAVE BEEN DEFINITIVELY ESTABLISHED FOR A WARNING TO APPEAR IN THE LABELING. THERE NEED ONLY BE REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION WITH A DRUG, A STANDARD THAT COULD BE MET BY A WIDE RANGE OF EVIDENCE.

SO I THINK IT'S IN THAT LIGHT THAT WE HAVE TO START LOOKING AT THE EVIDENCE THAT THE DEFENDANTS BRING BEFORE US TODAY: THE EGAN ARTICLE, THE VICTOZA CITIZEN PETITION, AND THE LIKE. BECAUSE WHAT ALL OF THOSE THINGS SHOW, I WOULD CONTEND, IS THAT THE FDA CONCLUDED THAT AS OF THAT MOMENT, BASED UPON THE SCIENCE THEY HAD SEEN, A PANCREATIC CANCER WARNING WAS NOT REQUIRED. THEY DID NOT CONCLUDE THAT ONE WOULD NOT BE PERMITTED.

AND I WOULD BE HAPPY TO DO THIS IF THE COURT WANTS, BUT I THINK YOU ARE BOTH INTIMATELY FAMILIAR WITH THE EGAN ARTICLE, WITH THE CITIZEN PETITION. REPEATEDLY IN THOSE DOCUMENTS, THE FDA OFFICIALS MAKE CLEAR THAT THERE IS SMOKE HERE, THAT THEY HAVE LOOKED AT THIS EVIDENCE, THAT THE EVIDENCE

IS NOT SUFFICIENTLY COMPELLING AT THIS MOMENT FOR THEM TO MANDATE A WARNING. BUT THEY SAY WE'RE GOING TO CONTINUE LOOKING, THIS IS AN IMPORTANT ISSUE, THERE IS CLEARLY SOME SMOKE HERE, THERE IS DISPROPORTIONATE REPORTING AND THE LIKE.

DEFENDANTS' ARGUMENT THAT THE FDA'S FAILURE TO MANDATE MEANS NO CBE WOULD HAVE BEEN ACCEPTED ALSO PRESUPPOSES THAT THE SPONSOR'S VIEWS DON'T MATTER. BUT THEY DO.

AS DR. GOLDKIND, THE DEFENDANTS' EXPERT ON PREEMPTION, ADMITTED IN HIS DEPOSITION -- AND I'M SORRY. I DON'T HAVE THAT CITE IN FRONT OF ME, BUT I CAN GET IT FOR YOU, IF YOU WANT IT -- AS THE SUPREME COURT EXPLAINED IN *LEVINE*, THE FDA HAS LIMITED RESOURCES TO MONITOR THE SAFETY OF THE THOUSANDS OF DRUGS IT REGULATES. IT RELIES ON THE MANUFACTURER WHO HAS MORE RESOURCES TO DEVOTE TO A PARTICULAR DRUG, MORE INFORMATION ABOUT THE DRUG, AND BECAUSE OF THE THREAT OF TORT LIABILITY, MORE INCENTIVE TO ENSURE THAT ITS LABELING REMAINS CURRENT AND INCLUDES ALL APPROPRIATE WARNINGS. FOR THESE REASONS, OF COURSE THE FDA TAKES THE SPONSOR'S VIEWS REGARDING THE APPROPRIATENESS OF A WARNING INTO ACCOUNT.

AND THEN FINALLY, ON THESE BIG-PICTURE POINTS, DEFENDANTS' ARGUMENT THAT FDA'S FAILURE TO MANDATE A WARNING IS CLEAR EVIDENCE THAT THE FDA WOULD REJECT A CBE, ALSO RESTS ON THE FALSE PREMISES THAT IN BOTH CASES THE AGENCY WOULD BE ACTING FROM THE SAME BASE OF INFORMATION.

AS WE HAVE DOCUMENTED IN THE BRIEFING, THAT WOULD NOT

HAVE BEEN THE CASE HERE. THERE IS LOTS OF SIGNIFICANT EVIDENCE OF A CAUSAL RELATIONSHIP BETWEEN THE INCRETIN DRUGS AND PANCREATIC CANCER THAT FDA DOES NOT APPEAR TO HAVE BEEN AWARE OF OR CONSIDERED IN ITS REVIEW THAT LED TO PUBLICATION OF THE EGAN ARTICLE.

NUMEROUS CASES HOLD -- AND WE CITE THEM AT PAGES SIX AND SEVEN OF OUR OPPOSITION MEMORANDUM, INCLUDING THE *ACTOS* CASE, THE *DORSETT* CASE, THE *NEWMAN* CASE -- NUMEROUS CASES HOLD THAT THERE CAN'T BE CLEAR EVIDENCE WHEN THERE WAS NEW SAFETY INFORMATION AVAILABLE THAT WAS NOT CONSIDERED BY THE FDA.

AND BY CONTRAST, I SHOULD NOTE, IN THE *FOSAMAX* CASE -- ONE OF THE CASES IN WHICH THE FDA REJECTED A SUPPLEMENT TO ADD A WARNING AND THE COURT FOUND CLEAR EVIDENCE -- IN THAT CASE THERE WAS AN EXPLICIT FINDING BY THE COURT THAT DEFENDANT HAD PROVIDED ALL THE INFORMATION IT HAD TO THE FDA.

NOW, LET ME BE CLEAR ABOUT PLAINTIFFS' POSITION HERE BEFORE I TALK ABOUT ANY OF THAT NEW SAFETY INFORMATION. BECAUSE THE ISSUE IS NOT WHETHER DEFENDANTS FAILED TO PROPERLY DISCLOSE THIS INFORMATION TO THE FDA.

IN THE MDL, JUDGE BATTAGLIA, YOU HAVE MADE VERY CLEAR YOUR VIEW THAT *BUCKMAN* PRECLUDES THE COURT FROM TAKING ANY BREACH OF DEFENDANTS' FEDERAL REPORTING OBLIGATIONS INTO ACCOUNT, IN YOUR PREEMPTION ANALYSIS.

AS YOU KNOW, PLAINTIFFS DISAGREE WITH THAT ASSESSMENT. WE DON'T THINK IT CAN BE SQUARED WITH THE NINTH

CIRCUIT'S DECISIONS IN *MCCLELLAN V. IFLOW*, *STENGEL*, OR, INDEED, WITH *LEVINE* ITSELF, BUT THAT REALLY ISN'T THE ISSUE HERE.

THE ISSUE IS THAT THE FDA DIDN'T CONSIDER ANY OF THIS NEW INFORMATION IN ITS REVIEW -- NOT IN THE EGAN ARTICLE, NOT IN THE VICTOZA CITIZEN PETITION, NOT IN ANY OF THESE EVENTS THAT THE DEFENDANTS POINT TO AS CLEAR EVIDENCE. BUT DEFENDANTS COULD HAVE INCLUDED SUCH INFORMATION IN A CBE APPLICATION TO ADD A WARNING OR AN ADVERSE REACTION.

THE COURT: WHEN YOU SAY "INFORMATION," ARE WE TAKING SCIENTIFIC EVIDENCE OR SOMETHING ELSE?

MR. BOGRAD: WE'RE TALKING ABOUT SCIENTIFIC EVIDENCE OF DIFFERENT -- NO QUESTION, YOUR HONOR -- OF DIFFERING DEGREES OF STATISTICAL CERTAINTY, OF DIFFERING DEGREES OF PERVASIVENESS.

THE COURT: WE'RE TALKING DATA, SCIENTIFIC DATA, ESSENTIALLY?

MR. BOGRAD: DATA. SCIENTIFIC FINDINGS, INFORMATION. YES, YOUR HONOR.

THE COURT: OKAY. JUST TO MAKE SURE WE ARE ON THE SAME PAGE. GO AHEAD.

MR. BOGRAD: AND I ALREADY QUOTED THAT PASSAGE EARLIER ABOUT THE FACT THAT EVIDENCE TO SUPPORT A FINDING OF REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION CAN BE ALMOST ANYTHING.

WE HAVE CITED IN OUR PAPERS TO A NUMBER OF FDA

GUIDANCES THAT MAKE CLEAR THAT IT CAN INCLUDE SPONTANEOUS ADVERSE EVENT REPORTING, IT CAN INCLUDE CLINICAL TRIAL IMBALANCES, IT CAN INCLUDE NONCLINICAL ANIMAL STUDIES REGARDING THE DRUG, AND IT CAN -- ANYWAY, IT CAN INCLUDE ALMOST ANYTHING. WE HAVE MANY OF THOSE PIECES HERE.

LET ME START WITH THE CLINICAL TRIAL IMBALANCES. THE EGAN ARTICLE SAYS THE FDA REVIEWED CLOSE TO MORE THAN 200 CLINICAL TRIALS, EVEN THOUGH ACCORDING TO CLINICALTRIALS.GOV, I SHOULD NOTE, THERE WERE CLOSE TO 900 TRIALS INVOLVING THESE DRUGS. SO WHILE WE ARE NOT DISAGREEING THAT THIS WAS AN EXTENSIVE REVIEW THAT THE FDA UNDERTOOK, IT CERTAINLY DID NOT COVER THE UNIVERSE.

AND THEY SAID -- AND CLEARLY THE FDA, IN WRITING THE EGAN ARTICLE, HAD ACCESS TO THE STUDY THAT DR. ENGEL HAD DONE FOR MERCK, IN WHICH HE SAID -- THAT HE CONCLUDED THAT A POOLED ANALYSIS OF DATA FROM 14,000 PATIENTS WITH TYPE II DIABETES PROVIDED NO COMPELLING EVIDENCE OF AN INCREASED RISK OF PANCREATITIS OR PANCREATIC CANCER, AND DID THEY CITE THE PUBLISHED VERSION OF THAT STUDY IN THEIR PAPERS.

BUT THERE ARE A LOT OF OTHER CASES OF PANCREATIC CANCER IN THE TREATMENT ARMS OF CLINICAL TRIALS THAT WE ALREADY KNOW ABOUT, THAT WERE NOT REPORTED -- WELL, THAT ARE NOT INCLUDED IN THE STUDY. WHY THEY ARE NOT REPORTED, WE DON'T KNOW.

AS WE HAVE PRESENTED IN OUR PAPERS, THERE ARE AT

LEAST THREE CASES OF PANCREATIC CANCER, IN PATIENTS WHO USED SITAGLIPTIN IN CLINICAL TRIALS, THAT WERE EXCLUDED FROM THE ENGEL STUDY AND THAT WERE NOT PRESENTED TO THE FDA, WHICH ALTERS THE BALANCE BETWEEN THE DATA THAT ENGEL REPORTED, WHICH WAS THREE CASES IN THE TREATMENT ARM AND THREE IN THE CONTROL ARM, CHANGES THAT BALANCE FROM THREE TO THREE TO SIX TO THREE, A DOUBLING.

LIKEWISE, WE HAVE IDENTIFIED AT LEAST ONE CASE IN THE NOVO CLINICAL TRIALS THAT WAS NOT INCLUDED IN NOVO'S ANNUAL REVIEW REGARDING STATISTICAL IMBALANCE.

AND IN THE HEALTH CANADA MATERIALS, WHICH I WILL TALK ABOUT IN GREATER DETAIL IN JUST A MINUTE, HEALTH CANANDA'S STAFF IDENTIFIED ANOTHER SEVEN CLINICAL TRIAL CASES, THAT WHILE WE CAN'T BE COMPLETELY SURE, DON'T MATCH UP BY AGE OR GENDER WITH THE CASES THAT WE ALREADY KNOW ABOUT. SO THERE MAY BE YET ANOTHER SIX OR SEVEN CASES THAT THEY IDENTIFIED IN THEIR STUDIES.

I KNOW THESE ARE SMALL NUMBERS. WE'RE TALKING ABOUT A CONDITION THAT WHILE IT'S NOT RARE, OCCURS IN SMALL NUMBERS OF -- IN RELATIVELY SMALL NUMBERS ANNUALLY. THESE WERE MOSTLY SHORT-TERM CLINICAL TRIALS. THE NUMBERS ARE SMALL, BUT THEY ARE SIGNIFICANT. AND HAD THOSE NUMBERS BEEN PRESENTED TO THE FDA, I DON'T KNOW THAT ANYONE CAN SAY THAT IT WOULDN'T HAVE MADE A DIFFERENCE. INDEED, DEFENDANT'S EXPERT, DR. GOLDKIND, CONCEDED -- AND THIS IS -- I'M SORRY. I'M ABOUT TO USE SOME

EXHIBIT NUMBERS AND IT'S GOING TO BE CONFUSING BECAUSE THE WAY THE FEDERAL COURT HANDLES FILINGS, WHERE WE HAD THE DECLARATION OF MR. JOHNSON AS EXHIBIT 2 TO THE MOTION PAPERS; AND, THEREFORE, ALL OF HIS EXHIBIT NUMBERS AND ALL OF THE FILING EXHIBIT NUMBERS ARE DIFFERENT. SO I HAVE BOTH.

EXHIBIT 3 TO HIS DECLARATION IN THE MDL PROCEEDING, WHICH IS DOCUMENT FIVE UNDER PACER BECAUSE OF THE WAY THE SYSTEM CATEGORIZES IT, ARE OUR EXCERPTS FROM THE GOLDKIND DEPOSITION, WHERE HE RECOUNTS THE SIGNIFICANCE OF THIS INFORMATION AND SOME OTHERS.

THE EGAN ARTICLE ALSO TALKED ABOUT THE IMPORTANCE OF NONCLINICAL ASSESSMENTS AND REPORTED THAT MICROSCOPIC EXAMINATION FROM TOXICOLOGY STUDIES YIELDED NO FINDING OF OVERT PANCREATIC TOXIC AFFECTS.

BUT WE NOW KNOW THAT WASN'T TRUE. WE KNOW THAT THE PRIMATE STUDIES CONDUCTED BY AMYLIN AND LILLY -- AND PLEASE TELL ME HOW MUCH INFORMATION ABOUT THESE THINGS YOU WANT, BECAUSE I DON'T ACTUALLY THINK THE SUBSTANCE OF THE SCIENCE IS CRITICAL TO OUR DISCUSSION TODAY. AMYLIN AND LILLY'S PRIMATE STUDIES DID REVEAL OVERT PANCREATIC TOXIC EVENTS, ALTHOUGH DEFENDANTS DID NOT APPARENTLY REPORT THEM AS SUCH TO THE FDA.

BASED UPON PLAINTIFFS' EXPERT CLIVE TAYLOR'S BLIND ANALYSIS, THE CYNOMOLGUS MONKEY STUDY REVEALED HISTOPATHOLOGICAL FIGURES ASSOCIATED WITH PANCREATIC INJURY, INCLUDING BOTH INCREASED FREQUENCY AND HIGHER GRADE PANINS,

WHICH ARE INDICATORS OF PRECANCEROUS CHANGES. BUT THE DEFENDANTS REPORTED THE RESULTS OF THAT STUDY AS SHOWING ONLY HYPER-CELLULARITY.

LIKEWISE, IN AMYLIN AND LILLY'S BABOON STUDIES, DEFENDANTS OWN PATHOLOGIST, AS WELL AS DR. TAYLOR, RECOGNIZED THE DEVELOPMENT OF PANIN LESIONS, BUT DEFENDANTS SUBSTITUTED THE TERM "HYPERPLASIA" FOR PANIN BEFORE PUBLICATION AND SUBMISSION OF THE STUDY TO THE FDA, AND EXPRESSLY STATED THAT NO PANIN LESIONS WERE OBSERVED.

NOW, THESE ARE SIGNIFICANT FACTS. AGAIN, WOULD THEY CARRY THE DAY BEFORE THE FDA? WE DON'T KNOW. DR. GOLDKIND CONCEDES THAT IT'S SIGNIFICANT INFORMATION. HE ALSO, IN REPRESENTING HIS CLIENTS, SAYS I DON'T THINK IT WOULD MAKE A DIFFERENCE. BUT WE DON'T REALLY KNOW. WE HAVE TO SPECULATE.

SIMILARLY, NOVO NORDISK DID A POST-MARKETING STUDY INVOLVING ZDF RATS TREATED WITH EITHER LIRAGLUTIDE OR EXENATIDE, WHICH HAD BEEN REQUIRED BY THE FDA, AND REPORTED TO THE FDA THAT THEY FOUND NO EFFECTS ON OVERALL PANCREAS WEIGHT OR EXOCRINE AND DUCT CELL MASS PROLIFERATION.

THOSE STATEMENTS WERE CONTRADICTED BY FOLLOW-UP RESEARCH DONE INTERNALLY AT NOVO NORDISK, AND BY ITS CONTRACT RESEARCH ORGANIZATION, WHEN THEY WENT BACK AND LOOKED AT THE DATA AGAIN. AND AGAIN, WE HAVE NO INDICATION THAT THAT SUBSEQUENT FOLLOW-UP ANALYSIS WAS EVER REPORTED TO THE FDA. AND, AGAIN, DR. GOLDKIND SAID THIS INFORMATION WOULD BE

SIGNIFICANT TO THE FDA.

AND THEN LASTLY -- CAN YOU PUT UP THE FIVE PAGES FROM HEALTH CANADA -- OR PULL UP THE FIRST PAGE. I AM NOT GOING TO REVIEW THIS IN DEPTH. AND I KNOW WE HAVE HAD SOME DISAGREEMENTS ABOUT THE RELEVANCE OF FOREIGN REGULATORY INFORMATION.

HEALTH CANADA DID A -- SOMEWHAT SIMILARLY TO THE EGAN ARTICLE -- DID A SIGNIFICANT SIGNAL ASSESSMENT OF THE RISK OF PANCREATIC CANCER IN PATIENTS WHO HAD USED INCRETIN DRUGS. IT IS EXHIBIT 7 OR 10, DEPENDING ON WHICH SYSTEM YOU ARE USING TO COUNT, TO OUR MOTION PAPERS, THE MOTION IN SUPPORT OF PLAINTIFFS' AFFIRMATIVE MOTION.

AND I'M NOT GOING TO READ IT TO YOU. THIS IS PAGES 46 TO 50 THAT I CAN SHOW YOU IF YOU WANT TO SEE THEM. UNLIKE THE EGAN ARTICLE, WHICH IS A VERY BRIEF SUMMARY OF THE WORK THAT THE FDA HAD DONE, HEALTH CANADA PUBLISHED 98 PAGES IN AN EVALUATION OF THE RISK OF PANCREATIC CANCER AND FOUND -- AGAIN, I WON'T NECESSARILY READ THEM ALL -- BUT, YOU KNOW, INCRETINS HAVE BEEN SHOWN TO INCREASE PROLIFERATIONS AND TO HAVE ANTI-APOPTOTIC EFFECT; GLIPTINS INDUCE A CHRONIC INCREASE OF INCRETIN BLOOD LEVELS BY TWO-TO-THREEFOLD, AND HAVE BEEN ASSOCIATED WITH CELLULAR PROLIFERATION OF THE ENDOCRINE AND EXOCRINE COMPARTMENTS OF THE PANCREAS; ANIMAL STUDIES HAVE SHOWN THAT LONG-TERM EXPOSURE INDUCE DYSPLASIA AND THE DEVELOPMENT OF PANCREATITIS, ETC. ETC.

THIS GOES ON FOR FIVE PAGES. AND THE BOTTOM LINE, AS WE ALL KNOW, IS THAT HEALTH CANADA RECOMMENDS THAT A WARNING NEEDS TO BE ADDED.

NOW, SO FAR AS WE KNOW THIS MORNING, WE KNOW THAT MERCK HAS HAD SOME SUBSEQUENT COMMUNICATIONS WITH HEALTH CANADA. WE DON'T KNOW THE NATURE OF THOSE COMMUNICATIONS BECAUSE THEY OCCURRED AFTER -- SOME OF THEM OCCURRED AFTER THE DISCOVERY DATE. SO FAR AS WE KNOW, THE ADDITION -- THIS HAS NOT BEEN ADDED.

(PHONE DISTURBANCE/MUSIC PLAYING)

BUT THIS IS NEW SCIENTIFIC INFORMATION. THIS IS NOT JUST THE VIEWS OF ANOTHER FOREIGN REGULATORY AGENCY. IT IS A COMPILATION OF 98 PAGES OF DATA FROM A COMPREHENSIVE SIGNAL ASSESSMENT DONE BY A REPUTABLE REGULATORY AGENCY. NONE OF WHICH, SO FAR AS WE KNOW -- SOME OF WHICH UNDOUBTEDLY DUPLICATES SOME OF THE INFORMATION THAT DR. EGAN AND HER TEAM LOOKED AT, BUT MUCH OF WHICH DOES NOT APPEAR TO BE REFLECTED IN THE EGAN STUDY.

(PHONE DISRUPTION/MUSIC PLAYING)

THE COURT: I WAS PUTTING MY FINGER UP BECAUSE WE HAVE MUSIC AGAIN. CAN YOU TURN OFF THE MUSIC OR WE ARE GOING TO CUT YOU OFF AND NOBODY IS COMING BACK?

(PAUSE)

OKAY. IT SOUNDS LIKE IT'S GONE. ALL RIGHT. CONTINUE, SIR.

MR. BOGRAD: ANYWAY, I WOULD URGE THE COURT TO FOCUS ON -- RATHER THAN READING ALL 98 PAGES, WE PROVIDED THEM TO YOU, PAGES 46 TO 50, WHICH ARE THE SUMMARY AND CONCLUSIONS IN WHICH THEY COME TO THE CONCLUSION THAT THERE IS EXTENSIVE EVIDENCE OF A CAUSAL RELATIONSHIP, THAT AT LEAST IN HEALTH CANADA'S VIEW SUPPORTED THE ISSUANCE OF THE INCLUSION OF WARNING ABOUT PANCREATIC CANCER ON LABELING.

ALL OF THIS IS PRECISELY THE SORT OF NEW SAFETY INFORMATION THAT THE FDA SAYS CAN AND SHOULD BE CONSIDERED IN CHANGES TO LABELING, AND CAN AND SHOULD BE PRESENTED IN SUPPORT OF CHANGES BEING EFFECTED SUPPLEMENT, TO ADD A NEW WARNING.

THE COURT: ARE YOU SUGGESTING THE CONCLUSIONS OF HEALTH CANADA? WHAT ABOUT THE DATA?

MR. BOGRAD: I'M TALKING SPECIFICALLY ABOUT THE DATA, YOUR HONOR. I DO THINK THE FDA TAKES THE VIEWS OF FOREIGN REGULATORY AGENCIES INTO ACCOUNT. INDEED, THE EGAN ASSESSMENT SHOWS THAT THEY CARED ABOUT WHAT THE EUROPEAN MEDICAL AGENCY THOUGHT IN THIS INSTANCE. SO I THINK THEY WOULD HAVE BEEN INTERESTED IN KNOWING THAT A FOREIGN REGULATORY AGENCY HAD REACHED A CONTRARY CONCLUSION.

BUT WHOLLY APART FROM THAT, THERE IS OODLES AND OODLES OF DATA THROUGHOUT HEALTH CANADA THAT IS NOT REFLECTED IN THE EGAN ARTICLE. SO WE DON'T KNOW WHETHER THAT INFORMATION WAS EVER PROVIDED TO THE FDA. WE SEE NO INDICATION THAT IT WAS. AND THERE IS LOTS OF INFORMATION IN THERE THAT IS NOT

REFLECTED IN THE DATA INCORPORATED INTO THE EGAN ARTICLE. ALL OF THAT, WE CONTEND, IS RELEVANT, NEW SAFETY INFORMATION THAT WOULD HAVE SUPPORTED A CBE.

THE COURT: AND TO BE FAIR, WE DON'T KNOW THE TOTALITY OF THE 200-OR-SO STUDIES BY NAME THAT THE FDA LOOKED AT. WE KNOW THE ONES THEY REFERRED TO.

MR. BOGRAD: THAT'S CORRECT, YOUR HONOR.

THE COURT: ALL THE REST IS WHAT IT IS.

MR. BOGRAD: I THINK WE DO KNOW -- AND I'M NOT THE PERSON WHO IS MOST FAMILIAR WITH THE DISCOVERY IN THIS CASE. I DO THINK IN SOME INSTANCES WE HAVE LISTS OF WHICH PARTICULAR TRIALS WERE IDENTIFIED TO THE FDA. THAT IS HOW WE KNOW THAT THE LIST THAT MERCK SENT TO THE FDA LEFT OUT THE THREE STUDIES THAT HAD THOSE THREE POSITIVE CASES OF PANCREATIC CANCER THAT I MENTIONED EARLIER. BUT WE DON'T KNOW WHAT THE UNIVERSE OF CASES WAS. AND WE DON'T KNOW.

BUT THAT ACTUALLY BRINGS ME TO MY POINT. ESPECIALLY IN LIGHT OF THE FACT THAT THE FDA REPEATEDLY SAYS IT HASN'T REACHED A DEFINITIVE CONCLUSION REGARDING A CAUSAL RELATIONSHIP, ALL OF THIS NEW SAFETY INFORMATION COULD WELL HAVE LED THE FDA TO APPROVE THE CBE.

WE DO NOT UNDERSTAND THE DEFENDANTS TO DISPUTE THAT THE FDA DIDN'T HAVE OR DIDN'T CONSIDER THIS SAFETY INFORMATION. MAYBE THEY DISPUTE SOME PIECE OF IT. I DON'T KNOW. THEY HAVE NOT TO DATE. NOR THAT THEY COULD HAVE INCLUDED IT -- NOR DO

THEY DISPUTE THAT THEY COULD HAVE INCLUDED IT IN SUPPORT OF A CBE. INSTEAD, THEY SIMPLY ASSERT THAT WE HAVE TO SPECULATE ABOUT WHETHER IT WOULD MAKE A DIFFERENCE.

DR. FLEMING CERTAINLY SAYS IT WOULD HAVE. HE SAYS HE HAS NO DOUBT THAT A CBE WOULD HAVE BEEN APPROVED. DR. GOLDKIND SAYS I CAN'T IMAGINE IT WOULD HAVE MADE A DIFFERENCE GIVEN THE EXTENSIVE STUDY THAT DR. EGAN ENGAGED IN. I CALL THOSE BOTH SELF-SERVING ANSWERS BY THE EXPERTS ON BEHALF OF THEIR CLIENTS THEY SERVE.

THE COURT: THAT'S WHAT EXPERTS ARE SUPPOSED TO DO. (LAUGHTER)

MR. BOGRAD: THAT IS EXACTLY WHAT EXPERTS ARE SUPPOSED TO DO, YOUR HONOR. BUT WE DON'T KNOW, AND THAT'S THE POINT. WE HAVE TO SPECULATE ABOUT WHAT WOULD HAPPEN IF A PROPERLY SUPPORTED CBE HAD BEEN SUBMITTED. AND BECAUSE WE HAVE TO SPECULATE, WE WIN.

THE WHOLE POINT OF THE CLEAR EVIDENCE ANALYSIS IS IF THERE IS DOUBT ABOUT HOW THE FDA WOULD HAVE RESPONDED -- AND THIS IS WHY I DON'T DISAGREE WITH DEFENDANTS THAT THERE ARE UNDOUBTEDLY WAYS OTHER THAN BY REJECTION OF A CBE THAT YOU COULD ESTABLISH CLEAR EVIDENCE. I AM SURE THERE ARE.

AS I SAID, IN THE *DOBBS* CASE, THERE WAS A REJECTION OF EITHER A CBE OR A PRIOR APPROVAL SUPPLEMENT, BUT THERE WAS ALSO AN EXPLICIT ORDER FROM THE FDA THAT SAID, YOU KNOW, PUT THIS STATEMENT ON YOUR LABEL THAT IS INCONSISTENT WITH THE

PLAINTIFFS' THEORY OF LIABILITY. I DON'T DOUBT THAT THAT IS CLEAR EVIDENCE.

BUT WHERE THERE IS DOUBT IT CUTS IN PLAINTIFFS' FAVOR ON THE PREEMPTION DEFENSE. BECAUSE THE WHOLE POINT OF THE PREEMPTION DEFENSE IS THE EVIDENCE MUST BE CLEAR THAT IT WOULD HAVE BEEN IMPOSSIBLE FOR DEFENDANTS TO ADD THE WARNING.

NOW, OF COURSE IT WAS IMPOSSIBLE. THE WHOLE POINT OF A CBE IS THEY COULD PUT IT ON THE LABEL TOMORROW AT THE SAME TIME THEY TELL THE FDA, AND THEN WAIT FOR THE FDA TO ACT. BUT WE AGREE THAT IF THE FDA THEN SAID YOU HAVE TO TAKE THAT OFF, THAT COUNTS AS IMPOSSIBILITY. BUT WE DON'T KNOW WHAT THE FDA WOULD HAVE DONE IF ONE OF THESE COMPANIES HAD COME TO THE FDA WITH A PROPERLY SUPPORTED CBE.

THE COURT: BUT IN YOUR ANALYSIS AS TO DOUBT, IT WOULD HAVE TO BE AT LEAST REASONABLE DOUBT TO THE EXTENT IT WOULD PRECLUDE A FINDING OF CLEAR EVIDENCE?

MR. BOGRAD: YES, SOME.

THE COURT: SOME DOUBT IS GOING TO HAPPEN IN EVERYTHING. WE ARE TALKING A REASONABLE DOUBT AS A FAIR WAY TO CHARACTERIZE YOUR STATEMENT?

MR. BOGRAD: RIGHT. I THINK, YOUR HONOR, I WILL DRAW A DIFFERENT ANALOGY BECAUSE AS YOU KNOW WE HAVE AN AFFIRMATIVE SUMMARY JUDGMENT MOTION HERE, TOO, NOT JUST AN OPPOSITION TO THEIR SUMMARY JUDGMENT MOTION.

THE COURT: I KNOW.

MR. BOGRAD: AND I THINK THAT POINT YOU JUST MADE CONNECTS THE TWO VERY SLIGHTLY. AND I CERTAINLY DON'T INTEND TO SPEND A LOT OF TIME ON THE AFFIRMATIVE MOTION BECAUSE I THINK IT'S THE SAME QUESTION.

TO MY MIND -- AND THERE IS NO CASE LAW THAT SAYS THIS EXPLICITLY -- TO MY MIND, THE CLEAR EVIDENCE DEFENSE, THE PREEMPTION DEFENSE, IS CLASSICALLY A SUMMARY JUDGMENT DEFENSE. BECAUSE IF THERE IS A GENUINE DISPUTE OF MATERIAL FACT ABOUT WHAT THE FDA WOULD HAVE DONE WITH A PROPERLY SUPPORTED CBE, THEN NOT ONLY SHOULD DEFENDANTS' SUMMARY JUDGMENT MOTION BE DENIED, BUT OUR SUMMARY JUDGMENT MOTION TO REJECT THAT PREEMPTION DEFENSE SHOULD BE GRANTED. BECAUSE IF THERE IS A GENUINE DISPUTE, THERE CAN'T BE CLEAR EVIDENCE.

THE COURT: CORRECT.

JUDGE HIGHBERGER: ARE YOU SUPPORTING THE DEFENDANTS' THEORY THAT THIS REALLY IS A QUESTION OF LAW, HOWEVER?

MR. BOGRAD: NO, YOUR HONOR. I'M NOT SUPPORTING THEIR POSITION. I'M SAYING --

JUDGE HIGHBERGER: BECAUSE I PRESUPPOSE THAT THE QUESTION COULD BE PRESERVED FOR TRIAL AND A FACT-FINDER COULD ESSENTIALLY BE ASKED TO DETERMINE WHETHER OR NOT THEY COULD BE A QUALITY WEATHER FORECASTER AND DECIDE IF THERE WAS OR WAS NOT CLEAR EVIDENCE.

MR. BOGRAD: WELL, YOUR HONOR, LET ME DRAW A DISTINCTION. I THINK YOU'RE RIGHT, BUT IN THIS SENSE.

JUDGE HIGHBERGER: BUT YOU JUST SAID, NO, IT SHOULD BE RESOLVED IN SUMMARY JUDGMENT AND YOU NEVER SAID ANYTHING FOR TRIAL.

MR. BOGRAD: WELL, I THINK THE QUESTION OF WHETHER THERE IS A CLEAR EVIDENCE PREEMPTION DEFENSE SHOULD BE RESOLVED AND REJECTED RIGHT NOW. THAT IS WHY WE FILED AN AFFIRMATIVE MOTION. BUT, AT TRIAL, DEFENDANTS --

JUDGE HIGHBERGER: THAT IS WHAT IT MEANS, SO I DON'T HAVE OCCASION TO RULE ON THAT.

MR. BOGRAD: THAT IS CORRECT, YOUR HONOR. BUT BY CONTRAST, AT TRIAL, THE DEFENDANTS HAVE TO PROVE -- OR WE, THE PLAINTIFFS, HAVE TO PROVE CAUSATION. I ASSUME ONE OF THE WAYS IN WHICH DEFENDANTS COULD TRY TO PROVE THE ABSENCE OF SPECIFIC CAUSATION WOULD BE TO SAY THAT HAD THE DEFENDANTS GONE TO THE FDA, THE FDA WOULD HAVE PROHIBITED THEM FROM PUTTING THE WARNING ON THE LABEL. I GUESS THEY COULD MAKE THAT ARGUMENT, AND MAYBE THE JURY WOULD BUY IT, AND MAYBE THAT WOULD BE THE BASIS ON WHICH THEY WOULD WIN THE CASE.

THE COURT: OR THE COURT WOULD GRAND IT ON A RULE 50 MOTION?

MR. BOGRAD: EXACTLY. I THINK THE ISSUE COMES UP. I JUST DON'T THINK YOU, AT THAT POINT -- AT THAT POINT I DON'T CHARACTERIZE IT AS PREEMPTION. I THINK OF IT AS A FINDING THAT PLAINTIFFS HAVE NOT PROVED ALL OF THE NECESSARY ELEMENTS OF THEIR CASE. BUT THIS IS PROBABLY A SEMANTIC ARGUMENT, AND I

DON'T THINK IT REALLY MATTERS. WHAT I'M SAYING IS IF THERE IS A GENUINE DISPUTE OF MATERIAL FACT ABOUT WHAT THE FDA WOULD HAVE DONE, THEN I THINK THEY LOSE THEIR PREEMPTION DEFENSE COMPLETELY, AND THEY CAN MAKE THIS OTHER ARGUMENT I JUST DESCRIBED AT TRIAL.

BUT YOU ARE CORRECT, YOUR HONOR. IN YOUR COURTROOM YOU DON'T HAVE TO DECIDE THAT QUESTION BECAUSE THERE IS NO AFFIRMATIVE MOTION. THERE IS ONLY THE DEFENDANTS' MOTION.

I THINK IT'S IMPORTANT TO LOOK AT WHAT THE EGAN ARTICLE SAYS. THE EGAN ARTICLE DOES NOT SAY WE WILL NOT PERMIT A DEFENDANT TO ADD A PANCREATIC CANCER WARNING. INDEED, IT LEAVES THE PANCREATITIS WARNING ON ALL OF THESE DRUGS.

AND I CONFESS, I GOT A LITTLE LOST IN MR. GOETZ' DISCUSSION OF PANCREATITIS AND HOW IT WAS SOMEHOW DIFFERENT FROM PANCREATIC CANCER. BECAUSE IT SEEMED TO ME, IF ANYTHING, THE FDA WAS SAYING THAT -- HE WAS SAYING THAT ADVERSE EVENT REPORT DATA WAS MORE VALID WITH REGARD TO PANCREATITIS. BUT THAT WOULD MEAN THAT THE EGAN CONCLUSION SHOULD HAVE BEEN EVEN MORE CERTAIN THAT THERE WAS NO SIGNAL OF PANCREATITIS; AND, THEREFORE, EVEN MORE CERTAIN THAT PANCREATITIS SHOULD HAVE COME OFF THE LABEL THAN THAT PANCREATIC CANCER SHOULDN'T HAVE GONE ON.

I THINK THE BETTER EXPLANATION FOR WHY PANCREATITIS STAYED ON IS THIS DISTINCTION I HAVE BEEN DRAWING THROUGHOUT THIS ARGUMENT, ABOUT THE DIFFERENCE BETWEEN MANDATORY AND

PERMISSIVE. THE FDA LOOKED AT THE INFORMATION IT HAD AVAILABLE TO IT, WHICH, AS I'VE JUST EXPLAINED, WAS NOT EVERY PIECE OF INFORMATION THAT WAS OUT THERE. BUT THEY LOOKED AT THE INFORMATION THAT WAS AVAILABLE TO IT, AND THEY CONCLUDED THAT THERE WASN'T ENOUGH EVIDENCE FOR THEM TO COMPEL THE MANUFACTURERS TO ADD A PANCREATIC CANCER WARNING, NOR WAS THERE ENOUGH EVIDENCE FOR THEM TO SAY -- TO COMPEL THE MANUFACTURERS TO REMOVE THEIR PANCREATITIS WARNING. THEY SAID IT'S STILL INDETERMINATE. WE HAVEN'T REACHED A FINAL CONCLUSION.

THE COURT: BUT THEY DIDN'T POSE THE QUESTION OF WHETHER TO ADD IT OR REMOVE IT AS INDETERMINATE. THEY SAID IT WAS INDETERMINATE, BUT THERE WAS NO EVIDENCE OF A CAUSAL RELATIONSHIP BETWEEN THE DRUGS AND PANCREATIC CANCER.

MR. BOGRAD: THAT'S CORRECT, YOUR HONOR.

THE COURT: THERE WAS NEVER A QUESTION THAT I THINK YOU JUST POSED, UNLESS I MISUNDERSTOOD YOU.

MR. BOGRAD: NO. NO. BUT I'M SAYING BASED UPON THE FACT THAT THAT EVIDENCE WAS INDETERMINATE, THEY DID NOT FEEL THAT THEY HAD A SUFFICIENT FACTUAL BASIS TO MANDATE EITHER THE INCLUSION OF A PANCREATIC CANCER WARNING OR THE EXCLUSION OF A PANCREATITIS WARNING.

AND AS I SAID, THAT GOES BACK TO MY POINT RIGHT FROM THE BEGINNING: ALL OF THE CASE LAW SAYS THE FACT THAT THE FDA DOESN'T MANDATE DOESN'T MEAN THAT THERE IS CLEAR EVIDENCE THEY WOULD REJECT A VOLUNTARY CBE SUBMISSION BY THE COMPANIES.

THAT'S MOST OF WHAT I HAVE GOT. I DO WANT TO RESPOND TO A COUPLE OF THINGS THAT DEFENDANTS SAID IN THEIR ARGUMENT. FIRST, I WANT TO DEFEND DR. FLEMING A LITTLE BIT. I THINK WE ALL KNOW THAT DOCTORS AND DEPOSITIONS DON'T ALWAYS MIX WELL, AND HE CERTAINLY MADE SOME STATEMENTS THAT CAUSED US TO CRINGE A BIT. BUT I THINK IT'S VERY INTERESTING THAT IN ALL THOSE EXCERPTS, THEY CONVENIENTLY LEFT OUT SOME OF THE CONTEXT IN WHICH HE WAS MAKING SOME OF THESE STATEMENTS. I THINK IT'S VERY CLEAR THAT DR. FLEMING SAID, WELL, BOTTOM LINE, AT PAGE 16 OF OUR OPPOSITION SUMMARY JUDGMENT MOTION, DR. FLEMING SAID IT'S HIS VERY STRONG OPINION THAT A CBE WOULD HAVE BEEN APPROVED.

HE ALSO SAID THAT EGAN WAS UNPRECEDENTED, NOT BECAUSE IT WAS SOME NEWFANGLED SPECIAL AMAZING THING, BUT RATHER BECAUSE IT WAS SO ODD THAT IT WAS NOT THE KIND OF THING THAT, IN HIS VIEW, HAD TYPICALLY BEEN DONE WITHIN THE AGENCY.

AND HE SAID THAT, IN HIS MIND, THE EVIDENCE THAT THE AGENCY LOOKED AT WAS RIGHT AT THE THRESHOLD, RIGHT AT THE LINE BETWEEN, YOU KNOW, MANDATING A CHANGE TO THE WARNING OR NOT, WHICH IS ENTIRELY CONSISTENT WITH WHAT I JUST SAID ABOUT THE FACT THAT THE FAILURE TO MANDATE IS NOT SUBJECT TO THE SAME STANDARD OF REVIEW -- OR THE SAME LEGAL STANDARD AS A VOLUNTARY CBE SUBMISSION.

AND FINALLY, I HAVE TO TALK ABOUT THE SENTENCE THAT THEY MOST LOVED, WHERE HE SAID IT WOULD BE ABSURD TO PERMIT A

LABEL CHANGE AFTER THEY HAD JUST DONE THIS EGAN STUDY AND COME TO THIS CONCLUSION THAT THE LABELING WAS ADEQUATE.

THE QUESTION THAT HE WAS ASKED SPECIFICALLY SAID -- WAS A HYPOTHETICAL. AND IT SAID IF HAVING SEEN ALL OF THE DATA THAT WAS OUT THERE -- AND I'M SORRY. I DON'T HAVE IT RIGHT IN FRONT OF ME. I AM SURE I CAN PULL IT TO QUOTE TO YOU DIRECTLY -- BUT IT WOULD BE ABSURD, WOULDN'T IT, DR. FLEMING, WHERE YOU HAD ALL OF THE DATA THAT WAS OUT THERE AND AVAILABLE AND CONCLUDED THAT THE LABELING WAS ADEQUATE, TO THEN TURN AROUND AND LET THE DEFENDANTS PUT THE WARNING ON THE LABEL?

AND IN THAT NARROW CONTEXT, HE DID CONCEDE THAT THAT MIGHT BE ABSURD. A LITTLE BIT ABSURD, I THINK, IS HOW HE PUT IT.

SO AS I SAID, CONVERSELY, DEFENDANTS' EXPERT REPEATEDLY SAID WELL, GEE, ALL OF THIS EVIDENCE THAT PLAINTIFFS ARE POINTING TO THAT IT DOESN'T APPEAR THAT HEALTH CANADA CONSIDERED, IS SIGNIFICANT EVIDENCE OF PRECISELY THE KIND THAT I, IN MY EXPERIENCE, THE FDA CARES ABOUT AND WANTS TO SEE IN PASSING JUDGMENT ON A SUPPLEMENTAL LABELING APPLICATION.

SO I THINK WE CAN PICK AND CHOSE EXCERPTS FROM THE EXPERTS' TESTIMONY. AS I SAID, BOTTOM LINE, OURS SAID THE CBE WOULD HAVE BEEN APPROVED; THEIRS SAYS IT WOULDN'T. BUT THEY BOTH AGREE THAT THERE IS A LOT OF IMPORTANT INFORMATION HERE THAT DOESN'T APPEAR TO HAVE BEEN CONSIDERED BY THE FDA.

I WANTED TO TALK JUST FOR A SECOND ABOUT A COUPLE OF

THE CASES THAT DEFENDANTS MENTIONED. I'M SORRY. HERE IS THE QUOTE FROM DR. FLEMING, TO GO BACK.

HERE IS THE QUESTION: DO YOU AGREE WITH ME THAT IT WOULD BE ABSURD FOR THE FDA TO SAY WE'VE LOOKED AT ALL THE DATA, WE'VE DONE A COMPREHENSIVE EVALUATION, WE DON'T THINK THERE IS ANY EVIDENCE OF A CAUSAL ASSOCIATION, BUT GO AHEAD AND ADD A WARNING, ANYWAY?

AND I SUBMIT TO YOU THAT AS THAT QUESTION IS PHRASED, IT WOULD BE ABSURD. BECAUSE AS THAT QUESTION IS PHRASED, THE QUESTION IS ASKING WOULD THE FDA APPROVE A WARNING THAT HAD NO SCIENTIFIC BASIS BEHIND IT. AND THAT'S NOT THE QUESTION THAT IS BEING ASKED IN THIS CASE. AS I SAID, RIGHT AT THE TOP, WE ARE NOT ARGUING FOR A WARNING THAT WAS NOT JUSTIFIED BY THE SCIENCE. WE ARE ARGUING FOR A WARNING THAT IS.

DEFENDANTS MENTIONED A COUPLE OF CASES IN THEIR ARGUMENT THAT WERE NOT IN THEIR PAPERS. SEVERAL I HAVE ALREADY SPOKEN ABOUT. IN PARTICULAR, THE *RHEINFRANK* CASE, WHICH, LIKE SOME OF THE OTHERS, INVOLVES A SITUATION WHERE THERE WAS EITHER A CBE OR A PRIOR APPROVAL SUPPLEMENT EXPRESSLY DENIED BEFORE THE FDA BEFORE THE COURT FOUND CLEAR EVIDENCE.

BUT I WAS SURPRISED WHEN THEY MENTIONED THE *RECKIS* CASE BECAUSE MY FIRM FILED AN AMICUS BRIEF IN THAT CASE. IT WASN'T MY BRIEF SO I WASN'T IMMEDIATELY FAMILIAR WITH IT, BUT I WAS PRETTY SURE THE CASE HAD UPHELD A $50 MILLION VERDICT FOR THE PLAINTIFFS. SO IT SEEMED VERY ODD THAT THEY WERE CITING IT

AS A COMPELLING CASE OF CLEAR EVIDENCE.

AND IT'S TRUE THAT THERE IS A VERY SMALL PIECE OF THE CASE IN WHICH THE COURT SAYS THE FDA HAD DENIED A PETITION TO ALLOW IN REFERENCES TO STEVENS JOHNSON SYNDROME AND TOXIC EPIDURAL NECROSIS ON THE LABELING FOR AN OVER-THE-COUNTER -- WAS IT IBUPROFEN?

MR. KENNERLY: CHILDREN'S MOTRIN.

MR. BOGRAD: CHILDREN'S MOTRIN. AND SO THEY DROPPED THAT PART OF THE CLAIM. BUT THE FOCAL POINT OF PLAINTIFFS' CLAIM WAS A DIFFERENT PIECE THAT THE FDA HAD NOT DIRECTLY CONSIDERED IN THE CITIZEN PETITION AND, AS I SAID, LED TO THE AFFIRMANCE OF A 50-MILLION-DOLLAR VERDICT.

BUT THE IMPORTANT POINT FOR PRESENT PURPOSES GOES TO THE IMPORTANT DISTINCTION BETWEEN A CBE APPLICATION AND A CITIZEN'S PETITION. I AM QUOTING -- I HAVE ONLY BEEN ABLE TO PULL UP THE SLIP OPINION HERE ONLINE, SO I DON'T HAVE A CITE FOR YOU, BUT THIS IS PAGE 29 OF THE SLIP OPINION IN THE *RECKIS* CASE: MOREOVER, BECAUSE THE DEFENDANTS WERE NOT INVOLVED IN THE SUBMISSION OF THE CITIZEN PETITION, THE ABSENCE OF THE FDA'S EXPLICIT REJECTION OF THE PHRASE "LIFE-THREATENING DISEASES" OR ANY RATIONALE FOR THE DECISION NOT TO REQUEST THAT MANUFACTURERS ADD SUCH A WARNING TAKES ON INCREASED SIGNIFICANCE.

SO THAT IS SAYING THE FACT THAT THEY DIDN'T ADDRESS SOMETHING IN THE CITIZEN PETITION BECOMES EVEN MORE

IMPORTANT -- THAT IS, EVEN ASSUMING FOR SAKE OF ARGUMENT THAT WE COULD PREDICT THE FDA WOULD HAVE REJECTED A CITIZEN PETITION PROPOSAL TO ADD ONLY THIS WARNING, THAT WOULD NOT ANSWER THE QUESTION WHETHER THE FDA WOULD HAVE REJECTED THE WARNING HAD IT BEEN SOUGHT BY THE DEFENDANTS THEMSELVES.

AND I CITE TO A CASE THAT IS IN OUR PAPERS, CALLED *SCHEDIN V. ORTHO-MCNEIL-JANSSEN,* PARENTHETICAL, FDA'S DECISION NOT TO SEEK LABEL CHANGE IN THE FACE OF A CITIZEN'S PETITION NOT SUPPORTED BY THE DRUG MANUFACTURER DOES NOT CONSTITUTE CLEAR EVIDENCE THAT THE FDA WOULD HAVE REJECTED A LABEL CHANGE PROPOSED BY THE MANUFACTURER.

AND THEN THEY CITE THE *DORSETT* CASE FROM THE CENTRAL DISTRICT OF CALIFORNIA FOR THE SAME PROPOSITION. AND THEY CONCLUDE WITH A QUOTE FROM *WYETH V. LEVINE* THAT THIS IS SO BECAUSE IT'S ABSURD -- OR THE VERY IDEA THAT THE FDA WOULD BRING AN ENFORCEMENT ACTION AGAINST A MANUFACTURER FOR STRENGTHENING A WARNING PURSUANT TO THE CBE REGULATION IS DIFFICULT TO ACCEPT.

THE COURT: BUT IF THE CBE WARNING WAS UNSUPPORTED BY ANY EVIDENCE, THEN IT WOULD CREATE A MASSIVE IMPACT UPON THE WELL-BEING OF PATIENTS, POTENTIALLY, WHO MIGHT SUSPEND TREATMENT IN THE FACE OF THIS WARNING. THE FDA MIGHT TAKE NOTICE AND DO SOMETHING.

MR. BOGRAD: YOUR HONOR, I'M SURE -- I DON'T KNOW IF THEY WOULD BRING A MISBRANDING ACTION, BUT THERE CERTAINLY HAVE

BEEN CBE PETITIONS THAT THE FDA HAS TURNED DOWN OR HAS GONE BACK TO THE MANUFACTURER AND SAID GEE, I DON'T LIKE THAT LANGUAGE; LET'S TRY THIS LANGUAGE INSTEAD.

WE DON'T KNOW. BUT THE WHOLE POINT IS WE DON'T KNOW WHAT WOULD HAVE HAPPENED IF A PROPERLY SUPPORTED CBE PETITION HAD BEEN FILED. AND BECAUSE WE DON'T KNOW, THERE IS NO CLEAR EVIDENCE THAT A CBE PETITION TO ADD A PANCREATIC CANCER WARNING WOULD HAVE BEEN REJECTED; THEREFORE, SUMMARY JUDGMENT SHOULD BE DENIED.

THE COURT: BUT WE DO KNOW THAT THE FDA AND THE EMA INDEPENDENTLY LOOKED AT THE STUDIES, LOOKED AT SLIDES, LOOKED AT TOXICOLOGY STUDIES, LOOKED AT THE NONCLINICAL ASSESSMENT DATA. I MEAN, IT'S NOT THAT THEY JUST ACCEPTED ALL OF THE DATA, IT SEEMS LIKE, AT FACE VALUE. THEY DID DO SOME INDEPENDENT ASSESSMENT. NOT EVERYTHING UNDER THE UNIVERSE, BUT THEY DID DO MORE THAN ACCEPT IT AS A GIVEN.

MR. BOGRAD: OH, YOUR HONOR, I SAY THERE IS SMOKE HERE IN FAVOR OF THERE BEING A PANCREATIC CANCER FINDING. THERE IS CERTAINLY SMOKE THE OTHER WAY THAT, YOU KNOW, WE MIGHT HAVE ENCOUNTERED TROUBLE -- OR, WE -- THEY MIGHT HAVE ENCOUNTERED TROUBLE IF THEY HAD FILED A CBE APPLICATION. THAT IS WHAT WE WILL BE FIGHTING ABOUT IF THE COURT ALLOWS US TO GET TO THE MERITS.

BUT DEFENDANTS ARGUMENT TURNS ON THE PREMISE THAT ONCE THE FDA DECLINES TO MANDATE A WARNING, YOU ARE PRECLUDED

FROM EVEN TRYING TO ADD IT THROUGH THE CBE PROCESS. AND THAT POSITION, WHICH THEY CONCEDE REPRESENTS A CHANGE IN THE LAW FROM *WYETH V. LEVINE* -- THAT POSITION, WE THINK, IS COMPLETELY UNTENABLE AND HAS BEEN REJECTED BY THE SUPREME COURT AND EVERY COURT TO CONSIDER IT.

SO I AM GOING TO STOP THERE AND INVITE MY COLLEAGUE -- I DON'T KNOW HOW MUCH TIME WE HAVE LEFT.

THE COURT: YOU HAVE EIGHT MINUTES.

MR. BOGRAD: I WILL INVITE MY COLLEAGUES, IF THEY WISH, TO ADD ANYTHING.

JUDGE HIGHBERGER: I HAVE A QUESTION FOR DEPEW OR CROOKE, BUT MAYBE KENNERLY WANTS TO TALK FIRST.

MR. KENNERLY: THEY CAN ANSWER THE QUESTION FIRST.

MR. DEPEW: I WILL ADDRESS ANY QUESTIONS THE COURT HAS.

JUDGE HIGHBERGER: OTHER THAN DELETING THE WORD "IRONCLAD" IN THE TENTATIVE, WOULD THERE BE ANY OTHER CHANGES YOU WOULD SUGGEST OUGHT TO BE MADE TO MY TENTATIVE?

MR. DEPEW: NO, YOUR HONOR.

JUDGE HIGHBERGER: NOW, YOUR COLLEAGUE, AND I DON'T HAVE HIS NAME MEMORIZED, SO I WILL JUST REFER TO HIM AS THE GENTLEMAN IN THE ARGUMENT, HAS LEFT ME SOMEWHAT CONFUSED, THOUGH, ON THE QUESTION OF WHETHER OR NOT A PREEMPTION CLAIM CAN SURVIVE TO BE A JURY TRIAL AS A QUESTION OF FACT.

WHAT I WAS HEARING FROM YOUR COLLEAGUE WAS SOMEHOW A

BELIEF THAT SOMEHOW IT HAS TO BE SO CLEAR, ONE WAY OR THE OTHER, THAT IT IS EITHER UNAVAILABLE AT THE TIME OF TRIAL OR IT SHOULD BE GRANTED BY SUMMARY JUDGMENT. WHEREAS I AM WILLING TO CONTEMPLATE THAT THIS IS LIKE SUBMITTING A QUESTION WHERE THE BURDEN OF PROOF IS CLEAR AND CONSEQUENCES, SAY, PUNITIVE DAMAGES. AND HERE WE, APPARENTLY, HAVE A VARIATION ON THE THEME. WE TELL THE JURY IT'S SUPPOSED TO BE A FINDING BY A CLEAR EVIDENCE, WHAT THE FDA WOULD HAVE DONE.

I THINK THAT COULD BE SAVED FOR TRIAL, BUT I WOUND UP CONFUSED AFTER I HEARD YOUR JOINT PLAINTIFF POSITION AS TO WHETHER OR NOT IT'S ACCEPTABLE BEING SAVED FOR TRIAL.

MR. DEPEW: ACTUALLY, I HAD A CONVERSATION WITH MS. CROOKE, ACTUALLY, DURING THAT PART OF THE ARGUMENT. AND WE BOTH THOUGHT THE SAME THING, THAT IT WOULD BE PRESERVED FOR TRIAL.

MR. BOGRAD: AS I SAID, YOUR HONOR, THEY WOULD STAND UP AFTER ME AND TELL ME WHAT I GOT WRONG.

JUDGE HIGHBERGER: OKAY. THEY MAY SPEND MORE IN TRIAL THAN CONSTITUTIONAL RIGHTS LITIGATORS DO.

I DON'T HAVE OTHER QUESTIONS, THEN. YOU CAN CERTAINLY ELABORATE, IF YOU WANT, OR IF YOU HAVE OTHER WORDS OF WISDOM.

THE COURT: MR. KENNERLY.

MR. KENNERLY: THANK YOU, YOUR HONOR. I JUST WANTED TO ADDRESS BRIEFLY THREE LITTLE ISSUES THAT WERE DISCUSSED UP

HERE. FIRST IS ABOUT THE SLIDES -- OF WHAT THE FDA ACTUALLY REVIEWED IN TERMS OF SLIDES.

THEY DID NOT DO A COMPREHENSIVE REVIEW OF THE UNDERLYING DATA OF THESE STUDIES. THE VAST MAJORITY THEY TOOK AT FACE VALUE. AND WHEN EGAN MAKES A REFERENCE TO REVIEWING SLIDES, ALL IT DISCUSSES IS THAT THEY REVIEWED 120 PANCREATIC HISTOPATHOLOGY SLIDES FROM ONE OF THE THREE SPONSOR-CONDUCTED RODENT STUDIES. THAT'S IT. WE KNOW FROM DISCOVERY WHICH STUDY THAT WAS. IT WAS AMYLIN'S RODENT STUDY BECAUSE WE HAVE THE REQUEST FROM THE FDA FOR THE SLIDES TO COME IN BLINDED TO THEM.

THAT'S ALL THE FDA INDEPENDENTLY REVIEWED OF THE SLIDES FOR HUNDREDS OF STUDIES OUT THERE. AND PART OF WHAT'S IN OUR BRIEF IS HOW NOVO'S OWN STUDY ON THAT EXACT SAME ISSUE, THE SAME POST-MARKETING REQUIREMENT, SHOWED DAMAGE TO THE PANCREAS, BUT THAT IS NOT WHAT THEY REPORTED TO THE FDA.

SO IN TERMS OF WHAT THE FDA LOOKED AT ON THAT, IT'S A MUCH MORE NARROW UNIVERSE THAN IT'S BEEN IMPLIED BY THE DEFENDANTS.

THE SECOND PART IS YOUR HONOR'S CONCERN ABOUT SUSPENDING TREATMENT. AND THAT WAS AN ISSUE IN THE SSRI CASES BECAUSE SSRIS WERE BY FAR THE BEST TREATMENT FOR DEPRESSION. AND PUTTING A SUICIDE WARNING ON SOMETHING THAT IS MEANT TO TREAT DEPRESSED PEOPLE IS VERY LIKELY TO DISSUADE THEM.

WE DON'T HAVE THAT SITUATION HERE. NOT IN THE LEAST. DEFENDANTS' DRUGS ARE NOT EVEN THEIR FIRST-LINE TREATMENT.

THEY ARE NOT EVEN THE SECOND-LINE TREATMENT FOR DIABETES. THE AMERICAN DIABETES ASSOCIATION HAS A GREAT CHART OF WHAT YOU DO WITH A DIABETIC PATIENT. YOU START OUT WITH METFORMIN, YOU CONSIDER INSULIN ON IT, AND THEN THERE IS AN ARRAY OF OPTIONS. THERE IS 13 DIFFERENT CLASSES OF DIABETES MEDICATIONS OUT THERE. THERE IS NO EVIDENCE, NO SUGGESTION BY THE FDA THAT SOMEHOW GLP-1 AGONISTS OR DPP-4 INHIBITORS ARE VASTLY SUPERIOR TO EVERY OTHER TREATMENT OUT THERE. THEY ARE NOT EVEN PRESCRIBED FIRST.

SO WE DON'T HAVE THAT SAME ISSUE, WHERE IF THE DEFENDANTS WARNED ABOUT PANCREATIC CANCER, THEN WE HAVE MILLIONS OF PATIENTS WITH DIABETES SUDDENLY HAVING NO TREATMENT. THEY SIMPLY MOVE TO A DIFFERENT FORM OF DIABETES TREATMENT THAT IS COMPARABLY EFFECTIVE.

AND THE LAST ISSUE THAT I WANTED TO COVER WAS -- TWO MORE ISSUES -- WAS THE TEMPORAL ASPECT OF THE DEFENDANTS CLAIM WE HAVE NEVER OBJECTED TO ANYTHING ABOUT PREEMPTION IN THE PAST.

AND OUR BRIEFING DID OBJECT TO THAT. WE'VE OBJECTED IT TO PREVIOUSLY. IT IS THEIR BURDEN TO SHOW PREEMPTION AT AN EARLIER TIME.

WHEN I DEPOSED DR. GOLDKIND, I ASKED HIM IF THE 2013 COMMUNICATION EVIDENCED ANY INTENT TO REJECT A CBE. HE SAID NO.

WHEN I TRIED TO TALK TO HIM ABOUT THE SUBSTANCE OF

EGAN AND WHAT IT REVIEWED, AND ASKED HIM, WELL, HOW WOULD YOU SAY THE FDA WOULD DO A REJECTION IN 2012? HE TOLD ME, WELL, I JUST KNOW IT WOULD BE.

I SAID HOW WOULD YOU KNOW WHAT THE DATA LOOKED LIKE AS IT WAS COMING IN AT DIFFERENT POINTS? AND HE FIRST IMPLIED THAT THE DATA MUST HAVE BEEN BETTER IN THE PAST.

AND WHEN I ASKED HIM, ARE YOU SAYING THERE IS INCREASING DATA SHOWING PANCREATIC CANCER? HE SUDDENLY BACKTRACKED AND THEN SAID HE JUST ASSUMES THE DATA ALWAYS LOOKS THE SAME AT ANY POINT IN THE PAST.

WELL, THAT'S NOT CORRECT. THAT'S OBVIOUSLY INCORRECT. THERE IS DIFFERENT DATA AT DIFFERENT POINTS. WE HAVE 2009, SEVERAL OF THE DEFENDANTS -- AMYLIN HAS ITS OWN SIGNAL DETECTION OF UNUSUAL ADVERSE EVENT REPORTING.

2011 WE HAVE THE ELASHOFF STUDY, FINDING ENHANCED RATES FOR THIS. SO THIS IDEA THAT WE CAN JUST EXTRAPOLATE BACK INTO THE PAST AT ANY POINT AND EXTRAPOLATE INTO THE FUTURE AT ANY POINT IS SIMPLY WRONG. WHAT THE DEFENDANTS HAVE HERE IS STUCK ON ONE DATE. THEY HAVE NO EVIDENCE. THEY ADMIT THEY HAVE NO EVIDENCE FOR ANYTHING AT A PRIOR POINT IN THE PAST.

THE LAST ISSUE I WANT TO TALK ABOUT WAS THE DATA ON HEALTH CANADA AND THEN I'M DONE, WHICH IS HEALTH CANADA, IN ESSENCE, HAS FOUR DIFFERENT CATEGORIES OF DATA THAT ARE NOT BEFORE THE FDA IN ANYTHING THAT WE CAN TELL. ONE IS HEALTH CANADA DID ITS OWN REVIEW OF THE WORLD HEALTH ORGANIZATION

ADVERSE EVENT DATABASE, WHICH IS DIFFERENT FROM THE FAERS. AND THEY FOUND, THROUGH THEIR OWN DATA MINING, INCREASED REPORTING OF THAT DATABASE, THERE IS NO EVIDENCE OF RECORD THAT THE FDA HAS EVER SEEN ANY ANALYSIS OR EVEN SEEN THE WORLD HEALTH ORGANIZATION DATA.

SECOND, HEALTH CANADA ASKED CANADA VIGILANCE AND THE OFFICE OF CLINICAL TRIALS TO LOOK FOR PANCREATIC CANCER CASES. WHAT THEY FOUND WAS IN THESE CLINICAL TRIALS SEVEN CASES. MERCK ITSELF WAS UNABLE TO IDENTIFY WHAT THESE CASES WERE. IT'S NOT THE SAME THAT THEY REFERRED TO IN ENGEL, AND IT'S NOT EVEN THE THREE THAT WE SAY WEREN'T REPORTED. IT'S A WHOLE OTHER CLASS OF CANCERS IN CLINICAL TRIALS. THE FDA HAS NO IDEA THIS DATA WAS OUT THERE, OR CERTAINLY DIDN'T AT THE TIME OF EGAN.

THE HEALTH CANADA ANALYSIS ALSO INCLUDES EIGHT ADJUDICATED POSSIBLE CAUSAL ASSOCIATIONS FROM ADVERSE EVENTS. THEY LOOKED INTO THEIR OWN PILE OF ADVERSE EVENTS COMING IN. THEY LOOKED SPECIFICALLY AT EACH ONE OF THEM, AND DID A VERY CONCRETE ANALYSIS AND FOUND THAT IN EIGHT OF THESE CASES THEY THOUGHT THERE WAS A POSSIBLE LINK TO THE MEDICATION.

NOW, THIS ISN'T JUST A RANDOM NUMBER THROWN OUT THERE. THIS IS HEALTH CANADA AND ITS OWN SCIENTIFIC GOING INTO THEIR OWN DATA, SPECIFICALLY MAKING A MEDICAL DETERMINATION THAT IT WAS POSSIBLY RELATED, AND THEN SUMMARIZING THAT DATA.

THE FDA DOES NOT HAVE THAT. THERE IS NO EVIDENCE OF

RECORD THAT THE FDA EVER HAD THAT.

THE LAST CATEGORY OF DATA SOUNDS LIKE A NONISSUE, BUT IT'S ACTUALLY CRITICAL TO THE CASE, WHICH IS THE HEALTH CANADA'S ANALYSIS CITES ALL OF ITS MEDICAL LITERATURE. WE KNOW HOW IT GETS TO WHERE IT'S GOING.

JUST LIKE HOW YOUR HONORS CAN'T KNOW EVERY CASE THAT IS RELEASED EVERYWHERE ON EVERY ISSUE, YOU RELY ON COUNSEL TO PRESENT IT TO YOU. THE FDA HAS THE EXACT SAME THING WITH THE DEFENDANTS. THEY DO NOT HAVE AN INCRETIN CLERK WHO IS WATCHING EVERY SINGLE STUDY THAT COMES OUT.

WE DON'T KNOW WHAT EGAN HAS LOOKED AT. WE KNOW THEY CAN'T BE LOOKING AT EVERY LAST LITTLE INCRETIN PAPER THAT COMES OUT THERE. SO WE DON'T EVEN KNOW THE UNIVERSE OF PUBLISHED DATA THAT THEY ARE LOOKING AT THERE. WHEREAS WITH HEALTH CANADA, WE HAVE A VERY LONG, DETAILED, CLEAR BIOLOGICALLY PLAUSIBLE MECHANISM THAT IS DESCRIBED THROUGH PUBLISHED LITERATURE THERE. AND WHEN WE ARE LOOKING AT WHAT THE FDA REVIEWED, WE CAN'T JUST ASSUME THAT THE FDA HAS REVIEWED ANY OF THOSE, OTHER THAN THE THREE PAPERS CITED IN EGAN.

SO WITH THAT, I WILL YIELD MY TIME.

THE COURT: A COUPLE QUESTIONS. JUST WITH ALL THIS INFORMATION, I WANT TO BE CLEAR. WHEN WAS THE HEALTH CANADA STUDY ISSUED AND WOULD HAVE BEEN AVAILABLE TO THE PUBLIC, INCLUDING THE FDA?

MR. KENNERLY: I DON'T THINK IT WAS ISSUED TO THE

PUBLIC. IT WAS A RESPONSE SENT BACK TO MERCK. I BELIEVE THE INITIAL SIGNAL ASSESSMENT IS OCTOBER 2013. AND THEN THERE IS CORRESPONDENCE BACK AND FORTH WITH MERCK AND HEALTH CANADA.

THE COURT: WELL, WHEN WAS THE DATA ABOUT THE EIGHT CANCER CASES SENT TO MERCK OR ANYONE ELSE?

MR. KENNERLY: OCTOBER 2013.

THE COURT: AND EIGHT OUT OF WHAT POPULATION?

MR. KENNERLY: THE POPULATION IS HARDER TO TELL BECAUSE THAT DATA RIGHT THERE IS NOT IN A CLINICAL TRIAL. HEALTH CANADA IS LOOKING AT ITS OWN ADVERSE EVENT REPORTING.

YOU KNOW, YOUR HONOR SAW FROM THE SAXENDA BRIEFING THAT THE FDA HAD LOOKED AT 49 OF THE FAERS CASES, WHICH IS, OBVIOUSLY, A TINY PIECE OF THE OVERALL REPORTS, BUT IT SEEMS THAT THE FDA ACTUALLY SPECIFICALLY LOOKED AT THOSE.

THIS IS SIMILAR WITH WHAT HEALTH CANADA IS DOING. THE POPULATION THERE IS THE WHOLE POPULATION OF CANADA. BUT HEALTH CANADA HAS SELECTED OUT SPECIFIC CASES TO TRY AND DETERMINE COULD THERE BE A CAUSAL RELATIONSHIP HERE.

THE COURT: THESE WERE EIGHT PEOPLE TAKING AN INCRETIN MIMETIC FOR A POPULATION OF EIGHT CANCERS OUT OF SOME DOUBLE-BLIND ANALYSIS OF ALL PANCREATIC CANCERS?

MR. KENNERLY: THEY WERE ALL TAKING INCRETIN MIMETICS. I BELIEVE THEY WERE ALL TAKING JANUVIA, BUT I DON'T KNOW THAT FOR CERTAIN BECAUSE HEALTH CANADA DID EXPAND ITS ANALYSIS TO INCLUDE SAXAGLIPTIN AND A DIFFERENT DRUG THERE THAT

IS NOT IN HERE.

MR. BOGRAD: SPECIFICALLY, YOUR HONOR, IT'S PAGE 48 OF THE HEALTH CANADA ASSESSMENT. THEY WENT THROUGH ALL THESE DATABASES, THEY IDENTIFIED 28 PANCREATIC CANCER CASES INVOLVING PATIENTS WHO HAD USED AN INCRETIN. 26 OF THEM BEING JANUVIA OR JANUMET, I THINK, AND TWO BEING SAXAGLIPTIN. AND THEN THEY DID THIS ANALYSIS THAT MR. KENNERLY IS TALKING ABOUT TO LOOK AT THE TIMING, LOOK AT THE DATES, LOOK AT THE CIRCUMSTANCES, AND TRY TO DETERMINE WHICH ONES WERE POTENTIALLY ACTUALLY CAUGHT, NOT JUST COINCIDENTLY OCCURRING IN PEOPLE WHO HAD TAKEN THE DRUG, BUT WHERE THERE WAS A REAL REASON TO THINK THAT IT MIGHT HAVE BEEN CAUSED BY THE DRUG. AND THAT IS HOW THEY GOT TO THE NUMBER OF EIGHT.

THE COURT: FROM THE U.S. STANDPOINT, IS THERE AN AGREED-UPON RATE OF INCIDENTS IN THE GENERAL POPULATION OF PANCREATIC CANCER THAT YOU MIGHT USE AS A MEASURING STICK, BAROMETER, OR ANY OF THOSE?

MR. KENNERLY: THERE IS A GENERALLY-AGREED RATE. BUT WHEN YOU ARE TALKING ABOUT ADVERSE EVENTS AND YOU ARE DOING THIS TYPE OF BIOSTATISTICAL PHARMACOVIGILANCE ANALYSIS, YOUR COMPARATOR IS REALLY TRYING TO FIND SIMILAR DRUGS OR SIMILAR PATIENTS FOR IT. SO YOU CAN'T REALLY DO THE NORMAL STATISTICAL REVIEW OFF IT.

THIS IS THE TYPE OF THING THAT DR. MADIGAN DID, WHICH IS WHAT YOU WANT TO LOOK AT IS FIND THE OTHER DIABETICS AND SEE

HOW FREQUENTLY THEY HAVE THIS. AND THAT IS WHAT DR. MADIGAN'S ANALYSIS SHOWS, WHICH IS YOU LOOK AT THESE DRUGS VERSUS ALL THEIR DIABETICS ON ANY TYPE OF MEDICATION AND THEY ARE JUST OFF THE CHARTS WITH THEIR REPORTING.

BUT THAT'S WHAT ADVERSE EVENT REPORTING IS. IT'S DESIGNED TO GENERATE A SIGNAL. IT'S INFORMATIVE OF CAUSAL ASSOCIATION. IT'S NOT DISPOSITIVE. NO ONE CONTENDS IT DOES. IT'S PART OF THE OVERALL PUZZLE.

ALTHOUGH FOR PURPOSES OF PREEMPTION, THE FDA GUIDANCE -- THIS IS EXHIBIT 5 TO OURS -- IS VERY CLEAR THAT TWO OF THE FACTORS FOR REASONABLE EVIDENCE OF CAUSAL ASSOCIATION ARE, ONE, THE FREQUENCY OF REPORTING; AND TWO, WHETHER THE ADVERSE EVENT RATE IN THE DRUG TREATMENT GROUP EXCEEDS THE RATE IN THE PLACEBO AND ACTIVE CONTROL GROUP.

IT SAYS NOTHING ABOUT STATISTICAL SIGNIFICANCE BECAUSE IF WE WAITED UNTIL STATISTICAL SIGNIFICANCE, WE WOULD NEVER HAVE A WARNING. THAT IS NOT REASONABLE EVIDENCE. THAT'S DISPOSITIVE EVIDENCE. REASONABLE EVIDENCE IS THESE THINGS THAT SET UP THE ALARM BELLS.

THE COURT: BUT WE HEARD FROM THE DEFENSE THAT THE SIGNAL IS, ESSENTIALLY, A HYPOTHESIS. IT'S THE ASSESSMENT OF THE UNDERLYING DATA FROM THE SIGNAL EVENT THAT IS SIGNIFICANT, NOT JUST THE SIGNAL ITSELF.

MR. KENNERLY: WELL, THAT IS WHERE DEFENDANTS ARE BLURRING TOGETHER WARNING AND PROOF OF GENERAL CAUSATION, WHICH

IS: A SIGNAL ALONE CAN GET A WARNING. THE FDA DOES NOT REQUIRE THAT YOU HAVE PROVED A CAUSAL LINK. IN FACT, THEY HAVE SAID EXACTLY THE OPPOSITE.

THE COURT: THEY TALK ABOUT REASONABLE EVIDENCE OF A CAUSAL LINK. THAT SEEMS TO BE SOME MODICUM OF PROOF AS OPPOSED TO WE'RE JUST GOING TO WARN BASED ON UNSUBSTANTIATED REPORTS.

MR. KENNERLY: WELL, IT IS SOME MODICUM OF PROOF EXCEPT THAT BY AND LARGE IN THE PAST, INCLUDING IN THESE DRUGS, WHEN YOU HAVE A WARNING OR AN ADVERSE REACTION ADDED, IT IS NOT THE RESULT OF STATISTICALLY SIGNIFICANT PROOF. IT'S THE RESULT OF ADVERSE EVENT REPORTING. THAT IS HOW PANCREATITIS GOT ON THERE IN THE FIRST PLACE. IT WAS NOT SHOWN STATISTICALLY IT HAS AN ELEVATED AMOUNT OF ADVERSE EVENT REPORTING.

RECENTLY THEY ADDED, TO ONE OF THESE, FLATULENCE BASED ON ADVERSE EVENT REPORTS THAT THEY SAID THEMSELVES. SO IF YOU ARE TALKING TO AN ONCOLOGIST ABOUT HOW DOES ADVERSE EVENT REPORTING INFORM PROOF, THEY WOULD SAY, WELL, IT KIND OF TELLS ME TO LOOK THIS WAY, BUT IT DOESN'T PROVE IT.

WHEN YOU ARE TALKING ABOUT A DRUG WARNING, THE WARNING HAS GOT TO GO ON THERE BEFORE YOU HAVE DISPOSITIVE PROOF. THAT'S THE WHOLE SETUP FOR IT, IS REASONABLE EVIDENCE IS DELIBERATELY SET BY THE FDA TO NOT BE FINAL PROOF, TO NOT BE MATHEMATICAL CERTAINTY, WHICH IS A REFERENCE TO NOT NEEDING STATISTICAL SIGNIFICANCE. IT'S SOMETHING THAT WOULD COMPEL YOU TO THINK THAT THIS WOULD MATTER TO A PHYSICIAN, THAT THIS COULD

BE THE DIRECTION THAT THINGS ARE GOING.

AND I THINK IT'S, AGAIN, IMPORTANT THAT THE FDA RELIES ON THE MANUFACTURERS. IT TELLS MANUFACTURERS IF YOU HAVE ANY DOUBT -- NOT JUST ONCE YOU REACH REASONABLE EVIDENCE -- IF YOU HAVE ANY DOUBT THERE IS REASONABLE EVIDENCE, BRING IT TO US AND WE CAN START TALKING ABOUT IT.

AND DEFENDANTS' EXPERTS ADMITTED THAT WAS THE STANDARD FOR IT, AND ALSO ADMITTED THAT IN THIS ENTIRE CASE THERE HAS BEEN ABSOLUTELY ZERO FROM THE DEFENDANTS TO FDA. THEY WANT TO SAY, WELL, WHY WOULD WE DO A CBE IF WE DON'T BELIEVE THERE IS REASONABLE EVIDENCE?

THE EVIDENCE HERE IS MORE THAN ENOUGH TO HAVE A DOUBT, WHICH IS THE ACTUAL STANDARD TO MOVE FORWARD WITH IT. AND, AGAIN, WHAT WE HAVE HERE IS A FRUSTRATION OF THE SYSTEM. IT'S SUPPOSED TO ORIGINATE FROM THE MANUFACTURERS, NOT WAIT FOR THE FDA TO MANDATE IT.

THE COURT: OKAY. WELL, THANK YOU. WHY DON'T WE TAKE OUR NEXT BREAK AND GIVE THE DEFENSE AN OPPORTUNITY TO STAGE ITS NEXT SET OF COMMENTS, AND WE'LL BE BACK IN TOWN.

(RECESS FROM 11:28 A.M. TO 11:41 A.M.)

THE COURT: AND WE HAVE RETURNED TO THE JOINT SESSION ON THE VARIOUS MOTIONS REGARDING PREEMPTIONS. AND WE ARE UP TO THE DEFENDANTS' REBUTTAL.

AND, MR. HEARD, I TAKE IT YOU WILL BE ADDRESSING YOUR FURTHER COMMENTS. IF YOU WOULD, IN THE PROCESS, IF YOU CAN

ADDRESS AT SOME POINT -- IT DOESN'T HAVE TO BE OFF THE TOP -- BUT THE LAST FDA ACTION, IF WE CONSIDER LABEL-RELATED ISSUES LATE 2014, NOW WE'RE LATE 2015. AND SO CAN WE STILL ACCOUNT, AT THIS DATE, FOR THE FACT THAT FROM YOUR VIEW THERE IS CLEAR EVIDENCE AGAINST A WARNING? AND SO IF YOU WOULD ADDRESS THAT.

AND I GUESS MOVING FORWARD, IF WE INDIVIDUALLY OR OTHERWISE DECIDE CLAIMS ARE PREEMPTED NOW, DOES THAT JUST KEEP SOME INDEFINITE FUTURE LIFESPAN UNTIL THE FDA MANDATES A CHANGE OR ONE OF THE DEFENDANTS COME UP WITH A CBE? THERE IS TWO QUESTIONS IN THERE, OF COURSE, AND IF OVER THE COURSE OF YOUR COMMENTS YOU COULD ADDRESS THOSE, I WOULD APPRECIATE IT.

BUT FOR NOW, I WILL LET YOU TAKE IT FROM WHERE YOU WOULD LIKE TO TAKE IT.

MR. HEARD: YOUR HONOR, I WILL ADDRESS THOSE, BUT IF I MIGHT, I WILL START IN A SLIGHTLY DIFFERENT PLACE, WHICH I THINK IS THE CORNERSTONE OF SEVERAL OF THE ARGUMENTS I WILL MAKE IN RESPONSE. AND I AM GOING TO TRY TO CEDE SOME TIME TO TWO OF MY COLLEAGUES ON SPECIFIC POINTS.

WHERE THE PLAINTIFFS GO FUNDAMENTALLY ASTRAY IS TO SUGGEST THAT THERE IS NO PREEMPTION BECAUSE AT SOME UNDEFINED POINT THERE WAS SOME UNDEFINED PIECE OF EVIDENCE THAT THE DEFENDANTS OR ONE OF THEM MIGHT HAVE TOSSED OVER THE THRESHOLD AS A CBE; AND THAT THE FDA MIGHT HAVE PERMITTED A LABELING CHANGE THAT IT OTHERWISE FOUND WAS NOT SATISFIED BY THE SCIENTIFIC EVIDENCE.

THAT TOTALLY DISREGARDS WHAT THE FDA HAS SAID REPEATEDLY. THERE IS NOT A SEPARATE STANDARD FOR SUBMITTING A CBE. THERE IS ONE STANDARD, ONE UNIFORM STANDARD FOR ALL LABELING CHANGES: THE INITIAL LABELING, SUBSEQUENT LABELING, WHETHER IT COMES FROM A MANUFACTURER, WHETHER IT COMES FROM THE FDA ITSELF AS A MANDATED CHANGE, WHETHER IT COMES IN A PRIOR APPROVAL SUPPLEMENT, WHETHER IT COMES IN A CBE-0 OR A CBE-30. IT'S ONE STANDARD. AND THAT STANDARD IS THAT THE CBE SUBMISSION MAY ONLY BE MADE WHEN THE EVIDENCE MEETS THE STANDARDS SET FORTH IN 201.57. EITHER REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION OR SOME REASON TO BELIEVE THERE IS A CASUAL RELATIONSHIP.

YET, EVERYTHING THE PLAINTIFFS SAID JUST NOW WAS THAT SOMEHOW THERE IS A LOWER SEPARATE STANDARD. SO THAT WHEN THE FDA SAYS THE SCIENTIFIC EVIDENCE DOES NOT MEASURE UP TO THESE THRESHOLD TESTS, THEY WOULD HAVE THE COURT BELIEVE THAT THE MANUFACTURER STILL COULD SUBMIT A CBE THAT WOULD BE APPROVED.

THAT IS TOTALLY CONTRARY TO THE FEDERAL REGULATIONS AND THE FDA'S INTERPRETATION OF THEM. AND FOR PRESENT PURPOSES ON PREEMPTION, IT MATTERS WHAT THE FDA WOULD CONCLUDE. AND THEY HAVE CONCLUDED THAT THE SCIENTIFIC EVIDENCE DOES NOT MEASURE UP. AND THEIR EXPERT AGREES THAT THE FDA HAS CONCLUDED THAT THE SCIENTIFIC EVIDENCE DOESN'T MEASURE UP.

THE NEW ENGLAND JOURNAL OF MEDICINE. IN THAT DOCUMENT, OR IN THE REJECTION OF THE CITIZEN'S PETITION, OR IN

THE BRIEFING BOOK, DOES THE FDA EVER SAY WE ARE NOT REQUIRING A LABELING CHANGE, BUT ONE IS PERMITTED?

HAVE THE PLAINTIFFS SHOWED YOU ANY DOCUMENT IN WHICH THE FDA MAKES A DISTINCTION BETWEEN MANDATING A CHANGE AND PERMITTING A CHANGE? NO. BECAUSE THERE IS ONE STANDARD MEASURED BY SCIENTIFIC PROOF.

MR. BOGRAD SAYS WE ARE ARGUING THERE IS A DEFINITE QUANTUM OF SCIENTIFIC EVIDENCE THAT MUST BE MET. NOT SO. WE'VE NEVER SAID THERE IS A QUANTUM OF EVIDENCE, BUT THERE IS A REGULATORY STANDARD FOR SUFFICIENT SCIENTIFIC EVIDENCE THAT IS PHRASED AS HAVING REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION OR SOME REASON TO BELIEVE THAT THERE IS A CAUSAL RELATIONSHIP. AND THE FDA HAS FOUND THAT ALL OF THE EVIDENCE THEY HAVE REVIEWED DOES NOT MEET EITHER STANDARD.

AND THEIR EXPERT AGREES THAT THE FDA HAS CONCLUDED THAT THE EVIDENCE DOES NOT MEET EITHER STANDARD.

SO WHAT DOES THAT LEAVE PLAINTIFFS WITH ARGUING? IT LEAVES THEM WITH SAYING, WELL, THERE IS EVIDENCE THAT WAS NOT DISCLOSED TO THE FDA. AND MR. BOGRAD SAYS -- AND I THINK I QUOTED THIS CORRECTLY -- LOTS OF SIGNIFICANT EVIDENCE OF CAUSAL RELATIONSHIP.

WHO SAYS? THE ONLY PERSON WHO SAYS THAT THERE IS LOTS OF EVIDENCE, IMPORTANT EVIDENCE OF CAUSAL RELATIONSHIP IS THE PLAINTIFFS' LAWYERS. THERE IS NO EVIDENCE IN THE RECORD THAT ANY OF THE EVIDENCE THEY TALK ABOUT IS SIGNIFICANT,

MATERIAL, WOULD CHANGE THE FDA'S DECISION. NO RECORD EVIDENCE.

BECAUSE YOUR HONOR, JUDGE BATTAGLIA, DISQUALIFIED DR. FLEMING IN MAJOR PART. BUT IN DOING SO YOU SAID -- AND YOU SAID YOU WOULD REDACT HIS REPORT YOURSELF -- AND DOING THAT YOU SAID THIS WILL PREVENT PLAINTIFFS FROM HAVING TO FIND A NEW EXPERT REGARDING FDA REGULATIONS, AND PERMIT THE PARTIES TO IMMEDIATELY MOVE FORWARD TO RETAIN FURTHER EXPERTS AS NECESSARY, IN RELATION TO THE ANTICIPATED PROCEDURE OF THIS CASE.

YOU PERMITTED THEM THE CHANCE TO NAME A NEW EXPERT WHO COULD SHOW THAT ANY OF THIS SUPPOSEDLY UNDISCLOSED INFORMATION IS MATERIAL, AND THEY DIDN'T COME FORWARD WITH AN EXPERT.

AND THEY ARE DEAD WRONG. DEAD WRONG THAT DR. GOLDKIND SAYS ANY THIS INFORMATION WOULD HAVE BEEN SIGNIFICANT TO THE FDA. HE SAYS JUST THE OPPOSITE. AND HE SAYS IT REPEATEDLY, AND HE EXPLAINS EACH OF HIS ANSWERS.

NOW, THERE IS A GOOD REASON WHY THE PLAINTIFFS DON'T EVER QUOTE OR PUT UP ON THE SCREEN ANYTHING DR. GOLDKIND SAYS, BECAUSE THEY WOULDN'T BE ABLE TO FIND ANYTHING THAT SUPPORTS THEIR ASSERTION. LET ME TAKE ONE EXAMPLE, PAGES 159 AND 160 OF HIS DEPOSITION, WHEN HE WAS ASKED ABOUT IMBALANCES IN SOME OF THE CLINICAL TRIAL DATA.

HE SAID: SO I BELIEVE THE TYPES OF IMBALANCES THAT YOU ARE REFERRING TO WOULD NOT BE GIVEN MORE WEIGHT THAN THE

DATA THEY HAVE.

AND AGAIN: FURTHER LARGE STUDIES WOULD BE NEEDED, IN MY OPINION, TO CHANGE THE FDA'S CURRENT CONCLUSION.

AND ON THE NEXT PAGE: I DON'T BELIEVE THAT THAT TYPE OF IMBALANCE WOULD CHANGE THE FDA'S ASSESSMENT, FOR THE REASONS THAT I'VE STATED.

AND HE GIVES REASONS FOR EACH CLASS OF DATA AS TO WHY THE FDA WOULD NOT TREAT THEM AS MATERIAL. AND BY AND LARGE IT ADDS UP TO SAYING GIVEN THEIR CONSIDERATION OF 250 TOXICOLOGY STUDIES WITH 18,000 ANIMALS, A COUPLE OF MORE INSTANCES OF PANCREATIC CANCER, IF THEY HAD THEM, ISN'T GOING TO CHANGE THE FDA'S OPINION.

BUT, OF COURSE, TAKE EACH CATEGORY EVIDENCE THE PLAINTIFFS HAVE TALKED ABOUT: ANIMAL DATA. THERE ARE NO INCIDENCES OF PANCREATIC CANCER IN ANY OF THE 18,000 ANIMALS.

AND IN THE DATA THAT PLAINTIFFS SAY WOULD CHANGE THE FDA'S MIND NOW, ARE THEY POINTING TO SUPPOSEDLY UNDISCLOSED DATA WITH PANCREATIC CANCER IN ANIMALS? NO. NOT A SINGLE INSTANCE.

THE FDA REVIEWED 200 CLINICAL TRIALS. IT FOUND NO TRIAL WITH A STATISTICALLY INCREASED INCIDENCE OF PANCREATIC CANCER. NOT ONE.

DO THE PLAINTIFFS NOW SAY THERE IS UNDISCLOSED DATA OF A STUDY IN WHICH THERE WOULD BE A STATISTICALLY SIGNIFICANT INCREASED RISK? NO, NOT ONE.

THE FDA POINTS TO TWO RANDOMIZED CLINICAL TRIALS, CARDIOVASCULAR TRIALS. YOU KNOW THE RESULTS IN THOSE TRIALS.

DO THE PLAINTIFFS POINT TO ANY DATA FROM CARDIOVASCULAR OUTCOME TRIALS THAT SHOWS AN INCREASED RISK? OF COURSE NOT. BECAUSE THEY KNOW THE TECOS STUDY, WHICH IS THE ONLY ONE THAT IS FULLY REPORTED AND COMES OUT OF *THE NEW ENGLAND JOURNAL OF MEDICINE*, REPORTS, AGAIN, THAT THERE ARE MORE INSTANCES OF PANCREATIC CANCER IN THE PLACEBO GROUP THAN THE STUDY GROUP.

SO WE NEED EVIDENCE -- WE NEED EVIDENCE THAT ANY OF THIS STUFF IS MATERIAL, NOT THE PLAINTIFFS' LAWYERS CONTEND IT IS. AND I MARK THEY HEDGED IN THEIR LAST BRIEF AND THEY ARE HEDGING NOW ABOUT WHETHER ANY OF THIS WAS UNDISCLOSED TO THE FDA. THEIR POSITION NOW IS, WELL, MAYBE IT WAS DISCLOSED. AND, INDEED, IT WAS IN THE CASE OF THE MERCK DATA.

THEY ARE SAYING BUT WE DON'T SEE ANY -- WE DON'T SEE ANY INDICATION, IN THAT *NEW ENGLAND JOURNAL OF MEDICINE* ARTICLE, THAT THE FDA SAID THEY CONSIDERED THIS AND THAT AND THIS EVIDENCE.

SO WE ARE FACED, THEN, WITH THE PARADOX THAT THE MORE MATERIAL THE FDA CONSIDERS AS PART OF ITS COMPREHENSIVE REVIEW OF THE SCIENTIFIC EVIDENCE, APPARENTLY THE MORE FOOTNOTES IT HAS TO PUT IN, THE LONGER THE REPORT HAS TO BE, IT HAS TO MENTION EVERY SINGLE PIECE OF DATA AND HOW IT CONSIDERED IT, OR ELSE THE PLAINTIFFS' POSITION WOULD BE GOTCHA, GOTCHA; THERE IS

SOME PIECE OF EVIDENCE WE CAN'T BE SURE THEY LOOKED AT OR ANALYZED.

THAT IS NOT THE TEST, I SUBMIT, THAT THE SUPREME COURT OFFERED. IT WANTED CLEAR EVIDENCE THAT THE FDA HAD FOCUSED ON THE SCIENTIFIC ISSUE, WAS LOOKING AT THE CURRENT SCIENTIFIC EVIDENCE. AND THERE IS NO DOUBT THAT THE FDA DID THAT HERE. IT'S NOT THE BUSINESS OF THE COURT TO SECOND-GUESS WHETHER THE FDA LOOKED AT EVERY PIECE OF DATA OR EXPLAINED EVERY PIECE OF DATA. IT'S SIMPLY TO KNOW THAT THEY ARE UP-TO-DATE, CURRENT, HAVE FOCUSED ON THE ISSUE.

HERE, THE COURT SHOULD HAVE NO DOUBT BECAUSE DR. FLEMING HIMSELF SAYS THIS IS A ROBUST EVALUATION, IT WAS AN UNPRECEDENTED COLLABORATION WITH THE EMA. THERE IS NO QUESTION THAT THEY CONDUCTED A SERIOUS STUDY OF THE DATA.

AND THAT, I SUBMIT, IS ALL THAT THE SUPREME COURT REQUIRES WHEN THE FDA THEN GOES ON AND COUPLES THOSE FINDINGS WITH THE CONCLUSION THAT THE LABELING IS ADEQUATE. ADEQUATE BECAUSE THERE IS NO SCIENTIFIC EVIDENCE THAT SAYS IT MEETS THE THRESHOLD FOR A CHANGE.

AND WE KNOW THAT THE FDA SPECIFICALLY CONSIDERED THE ADVERSE EVENT DATA AND SAID THAT DATA SUPPLIES NO NEW EVIDENCE THAT WARRANTS A CHANGE IN THE LABELING.

THE COURT: AND ISN'T THE ADVERSE REPORTING DATA PROBLEMATIC IN THE FDA'S EYES BECAUSE OF THE LONG LATENCY PERIOD WITH PANCREATIC CANCER IN THE FIRST INSTANCE?

MR. HEARD: YOUR HONOR IS ABSOLUTELY CORRECT AS TO WHY THERE IS A PANCREATITIS WARNING REFERENCING POST-MARKETING REPORTS, AND WHY THERE IS NOT A PANCREATIC CANCER WARNING OF THE SAME KIND.

IT IS PRECISELY BECAUSE -- AND WE -- LET ME JUST PULL THAT UP ONE MORE TIME: IT'S NOT POSSIBLE TO USE ADVERSE EVENT DATA TO SHOW A CAUSAL ASSOCIATION WHEN YOU HAVE HIGH-PREVALENCE BACKGROUND RATE AND UNTREATED POPULATION AND A LONG LATENCY PERIOD.

THE FDA HAS EXPLAINED WHY THERE IS A PANCREATITIS WARNING AND WHY THERE IS NOT A PANCREATIC WARNING. IT'S NOT OUR BUSINESS, THEN, TO SECOND-GUESS THE FDA WHEN WE KNOW THEY HAVE COME TO THIS CONCLUSION BASED ON THE MOST CURRENT SCIENTIFIC EVIDENCE.

NOW, THE SUMMARY JUDGMENT STANDARD. WE ARE AT COMPLETE ODDS. BUT I BELIEVE THAT OUR POSITION IS SUPPORTED BY EVERY SINGLE REPORTED CASE THAT HAS ADDRESSED PREEMPTION, WHETHER IT'S BEEN FOR PREEMPTION OR AGAINST PREEMPTION. AND THAT IS IF THE COURT KNOWS WHAT THE FDA HAS SAID AND DONE, THEN IT IS A QUESTION OF LAW WHETHER THAT CONSTITUTES CLEAR EVIDENCE.

EVERY ONE OF THESE DECISIONS -- *DORSETT*, *KOHO*, *GAETA* -- THEY ARE ON MOTIONS FOR SUMMARY JUDGMENT, OR THE COURTS ALLOWED A TRIAL RECORD TO BE ESTABLISHED AND THEN ADDRESSED THE ISSUE, AS A MATTER OF LAW, AS A MOTION FOR

JUDGMENT AFTER THE TRIAL. BUT IN EVERY CASE THE COURT HAS RESERVED FOR ITSELF WHETHER THE UNDISPUTED FACTS ADD UP TO CLEAR EVIDENCE.

JUDGE HIGHBERGER: YOU SEEM TO AGREE WITH MR. BOGRAD AT LEAST ON ONE POINT.

MR. HEARD: MAYBE SO. AND THERE IS NO DISPUTE HERE ABOUT WHAT THE FDA SAID AND DID. I HAVEN'T HEARD ONE YET. IT'S NOT IN THE BRIEFS. I THINK THAT IS WHY WE HAVE CROSS-MOTIONS FOR SUMMARY JUDGMENT.

ONE FINAL THING -- AND IT BACKTRACKS -- BEFORE I ADDRESS JUDGE BATTAGLIA'S QUESTIONS. THE PLAINTIFFS ARE FOND OF SAYING THAT THE MANUFACTURERS HAVE RESPONSIBILITY FOR THE LABELING. THEY ARE RESPONSIBLE FOR MAKING AN INDEPENDENT JUDGMENT ABOUT WHETHER THE EVIDENCE MEETS THE STANDARD FOR A LABELING CHANGE. AS THE SEVENTH CIRCUIT SAID IN *MASON*, IT IS A VIOLATION OF FEDERAL LAW TO SUBMIT A CBE THAT IS NOT SUPPORTED BY REASONABLE EVIDENCE.

WHEN EXACTLY AND WHAT EXACTLY DO THE PLAINTIFFS SAY THE MANUFACTURER SHOULD HAVE DONE? BEFORE 2013 IN THE DRUG SAFETY COMMUNICATION, WAS THERE A SAFETY SIGNAL THAT CALLED FOR THE MANUFACTURERS TO SUBMIT A LABELING CHANGE? NOT ACCORDING TO DR. FLEMING.

I'M NOT SAYING THAT ON THE BASIS OF *BUTLER* -- HE BEGINS SENDING ARTICLES IN 2009, 2010 AND -- I'M NOT SAYING A CBE SHOULD HAVE BEEN SUBMITTED BASED ON *BUTLER*.

MARCH 2013 THE FDA ISSUES ITS DRUG SAFETY COMMUNICATION. IMPORTANT POINT OF CHRONOLOGY HERE. THE FDA ISSUES THAT DRUG SAFETY COMMUNICATION BASED ON UNPUBLISHED DATA. THEY HAVE IT. THE DEFENDANTS DON'T. THAT DATA ISN'T PUBLISHED UNTIL EIGHT DAYS LATER, ONLINE.

SO SHOULD THE MANUFACTURERS HAVE BEEN DOING WHAT THE FDA DID IN ITS 2013 DRUG SAFETY COMMUNICATION? THEY COULDN'T HAVE BECAUSE THEY DIDN'T HAVE WHAT THE FDA HAD THAT SET THE FDA IN ACTION.

SO ARE THE PLAINTIFFS SAYING THAT AFTER THE FDA ISSUED ITS DRUG SAFETY COMMUNICATION ON MARCH 14, 2013, SHOULD WE HAVE SUBMITTED A CBE THEN? OR ISN'T THAT A PRIME CASE OF DOING A FUTILE ACT, WHICH THE LAW SAYS NO ONE IS REQUIRED TO PERFORM. THE FDA HAD SAID IT WAS GOING TO BE LOOKING AT THE ISSUE AND REPORTING BACK. THAT WAS NO TIME TO SUBMIT A CBE.

WELL, AND IF WE HAD SUBMITTED A CBE, BASED ON WHAT EVIDENCE? ONE DOESN'T KNOW BECAUSE FLEMING SAYS THERE WASN'T ANY THAT WOULD HAVE JUSTIFIED ONE. DOESN'T THE FDA'S *NEW ENGLAND JOURNAL OF MEDICINE* ARTICLE TELL US AT THAT POINT THAT UP TO THAT TIME, BASED ON ALL THE EVIDENCE, THERE WAS NO SCIENTIFIC BASIS FOR MAKING A LABELING CHANGE BY CBE OR ELSEWISE?

NOW, THAT BRINGS US TO YOUR HONOR'S QUESTION. WHAT MIGHT HAPPEN NOW? MIGHT NEW EVIDENCE COME OUT AND MIGHT IT CHANGE THE FDA'S OPINION?

OF COURSE. BUT THIS PREEMPTION ANALYSIS IS RETROSPECTIVE IN CHARACTER. WE ARE TALKING ABOUT PLAINTIFFS WHO TOOK THE DRUG IN THE PAST, WHERE THE ALLEGATION IS THAT THEY WERE NOT WARNED ADEQUATELY IN THE PAST. SO WE HAVE GOT A RETROSPECTIVE LOOK. IT NOW DOESN'T MATTER WHAT THE FDA DOES IN THE FUTURE AS TO THOSE PLAINTIFFS BECAUSE ALL THOSE PLAINTIFFS' CLAIMS ACCRUED SOME TIME AGO.

AND WHAT THE FDA HAS SAID IN 2014 -- AND THIS, I SUPPOSE, IS WHERE WE PART COMPANY WITH JUDGE HIGHBERGER. BASED ON WHAT THE FDA SAYS IN 2014 ABOUT ALL THE EVIDENCE, WE CAN LOOK BACK AND SAY THE FDA WOULD NEVER HAVE APPROVED A WARNING THAT WAS DIFFERENT, PRIOR TO THIS TIME.

I MEAN, I SAY THIS BASED UPON WHAT DR. FLEMING SAYS. I'M NOT SAYING BEFORE 2014 YOU SHOULD HAVE SUBMITTED A CBE. AND WHY NOT? BECAUSE EVEN HE CONCEDES THAT PRIOR TO THAT TIME THERE WASN'T EVIDENCE THAT MET THE THRESHOLD.

SO WHEN THE FDA NOW LOOKS AT THE LARGEST AMOUNT OF EVIDENCE -- THE UNIVERSE OF EVIDENCE -- AND SAYS THAT IS NOT ADEQUATE, WE CAN BE SURE THAT BASED ON LESSER EVIDENCE IN THE PAST THEY WOULD NOT HAVE DONE SO.

I THINK I LEFT OUT A SECOND ASPECT OF YOUR QUESTION. AND IF YOU RESTATE IT, I WILL TRY.

THE COURT: NO. I THINK YOU ACTUALLY COVERED IT. WHAT YOU ARE SAYING IS IF I FIND PREEMPTION AS OF FEBRUARY/MARCH 14TH, ANYONE WHO TOOK THE DRUG PRIOR TO THAT

TIME WOULD HAVE NO CLAIM AND WOULD BE PREEMPTED?

MR. HEARD: YES.

THE COURT: THE UNIVERSE OF CLEAR EVIDENCE INFORMATION WOULD BE LEFT FOR THE FUTURE. IT WOULD BE LEFT FOR SOME OTHER DAY WHEN SUCH EVIDENCE WOULD SURFACE. SOME ACTION WOULD BE TAKEN -- FURTHER INDEPENDENT STUDY BY THE FDA, A CBE BY A MANUFACTURER OR SOMETHING ELSE.

MR. HEARD: YES. THAT'S OUR POSITION. SO I WILL CEDE TO MR. GOETZ AND POSSIBLY TO MR. BROWN.

THE COURT: MR. GOETZ, GO AHEAD.

MR. GOETZ: THANK YOU. I WILL ONLY BE A MOMENT AND CEDE TO MR. BROWN. I WANTED TO ADDRESS TWO ISSUES. ONE WAS THE *WYETH V. LEVINE* QUOTE THAT I STARTED WITH, WHICH IS WE'RE DEALING WITH A CLEAR EVIDENCE STANDARD. AND I APPRECIATE JUDGE HIGHBERGER'S QUESTION TO MR. DEPEW ABOUT POTENTIALLY TAKING OUT "IRONCLAD." BUT I THINK IT'S EVEN MORE THAN THAT. I DON'T THINK IT'S A BEYOND-A-REASONABLE-DOUBT STANDARD, EITHER.

IF WE HAD PRESENTED CLEAR EVIDENCE, THAT IS ALL WE NEED TO DO. AND HERE WE HAVE AGREEMENT ON WHAT THE FACTS ARE. AND THE QUESTION BEFORE THE COURT IS A LEGAL ISSUE. AND MR. HEARD IS CORRECT ON THAT, I BELIEVE, THAT THIS IS A LEGAL ISSUE THAT YOU BOTH NEED TO ADDRESS.

IS THAT CLEAR EVIDENCE OF WHAT THE FDA WOULD DO? IT'S HARD TO IMAGINE CLEARER EVIDENCE THAN THE FDA ASSERTING IN *THE NEW ENGLAND JOURNAL ARTICLE*, THE EGAN ARTICLE ALONE, THAT

THE ASSERTIONS OF CAUSAL ASSOCIATION ARE INCONSISTENT WITH THE CURRENT DATA. AND WE HAVE GONE THROUGH MANY OTHER PIECES OF INFORMATION FROM THE FDA THAT LEAD TO THAT SAME CONCLUSION.

SO I COME BACK TO THE POINT THAT THE QUESTION BEFORE THE COURT ISN'T ARE THERE UNDISPUTED FACTS WHAT THE FDA WOULD DO, HAVE WE MET AN IRONCLAD STANDARD, OR HAVE WE MET A BEYOND-THE-REASONABLE-DOUBT STANDARD?

THE QUESTION -- AS PERHAPS UNSATISFACTORY AS IT IS BECAUSE THE SUPREME COURT SET FORTH THE STANDARD THAT IS SUPPOSED TO BE FLEXIBLE -- IS IS THERE CLEAR EVIDENCE? AND MY POINT IN CITING THE *WYETH* CASE ON THAT WAS THAT THE SUPREME COURT ACKNOWLEDGED THAT THERE ARE OTHER PARTIES THAT ARE AT ISSUE HERE. THERE ARE OTHER PARTIES, INCLUDING THE FDA AND THE MANY PEOPLE USING THIS DRUG, MANY PEOPLE WHO CAN'T USE OTHER DRUGS. WE'VE HEARD THAT THERE ARE OTHER DRUGS THAT ARE FIRST-LINE DEFENSES. WELL, THESE ARE PEOPLE WHO THOSE DRUGS DON'T WORK FOR.

THE OTHER POINT I WOULD MAKE IS MY CITATION OF *DOWHAL* AND THE *CROSBY* CASE WERE ON CONFLICT PREEMPTION. AND THE PLAINTIFFS IGNORED THAT THE WHOLE POINT OF THOSE CITATIONS WAS CONFLICT PREEMPTION. AND THIS IS AN INDEPENDENT REASON WHY, WHEN IN 2014 THE FDA SAYS -- AS IT DID IN *THE NEW ENGLAND JOURNAL* ARTICLE -- THAT THE DATA ARE INCONSISTENT WITH CAUSATION, THAT YOU CAN'T LET CASES GO FORWARD THAT WERE FILED THE DAY BEFORE OR A YEAR BEFORE, OR FOUR YEARS BEFORE BECAUSE

YOU'RE SENDING AN INCONSISTENT MESSAGE TO THE VERY PEOPLE THAT THE FDA ATTEMPTED TO, IN AN UNPRECEDENTED FASHION, SEND A CONSISTENT MESSAGE TO. THAT IS WHY IT WENT TO *THE NEW ENGLAND JOURNAL OF MEDICINE* RATHER THAN SENDING A HANDFUL OF LETTERS OUT TO US. IT WANTED A CONSISTENT MESSAGE OUT.

AND THE *DOWHAL* CASE AND THE *CROSBY* CASE ARE CALIFORNIA SUPREME COURT AND U.S. SUPREME COURT CASES ACKNOWLEDGING THE IMPORTANCE OF THIS CONFLICT PREEMPTION ISSUE.

AND I WILL TURN IT OVER TO MR. BROWN, UNLESS YOU HAVE QUESTIONS.

MR. BROWN: THANK YOU, YOUR HONORS. I WILL BE MUCH BRIEFER TODAY THAN I WAS ON WEDNESDAY. I HAVE A COUPLE RECORD CITES FOR YOU, JUST TO TRY TO SUPPLEMENT SOME OF THE POINTS THAT HAVE ALREADY BEEN MADE, BUT, HOPEFULLY, I WON'T BE TOO REDUNDANT HERE. I ALSO JUST WANT TO RESPOND TO ONE OR TWO POINTS, AT THE MOST, THAT WERE MADE BY THE PLAINTIFFS.

SO MR. HEARD ALREADY ANSWERED YOUR HONOR'S QUESTION ON SPONTANEOUS ADVERSE EVENT REPORTING. I CAN ANSWER ANY FURTHER QUESTIONS THAT YOU HAVE, IF YOU HAVE ANY.

BUT THE ONE ADDITIONAL PORTION OF THE RECORD I WOULD POINT OUT IS IN THE SAXENDA FDA BRIEFING DOCUMENT. ON PAGE 302 OF THAT DOCUMENT, THEY REINFORCE THE SAME POINT. AND THAT IS WHY SPONTANEOUS ADVERSE EVENT REPORTS, IN THIS CONTEXT, TO BE DISTINGUISHED FROM SOMETHING LIKE ACUTE PANCREATITIS OR ANOTHER CONTEXT, LIKE AN ACUTE SKIN REACTION OF SOME KIND. IT'S SIMPLY

NOT INFORMATIVE. SO WE HAVE HIM SAYING THAT BOTH --

JUDGE HIGHBERGER: THROUGH THE LATENCY PERIOD, IN PARTICULAR?

MR. BROWN: IT'S THE LATENCY PERIOD, BUT THERE ARE A NUMBER OF OTHER REASONS, YOUR HONOR. WHEN YOU HAVE AN EVENT THAT OCCURS FREQUENTLY IN THE BACKGROUND POPULATION, JUST GETTING A SINGLE REPORT ISN'T INFORMATIVE BECAUSE YOU HAVE TO HAVE A CONTROL GROUP, AND A VALID CONTROL GROUP. YOU ACTUALLY CAN'T JUST LOOK AT INCIDENT RATES FROM A DATABASE. YOU ACTUALLY NEED A TRIAL OR A VERY WELL-DONE OBSERVATIONAL STUDY.

AND THAT IS NOT ME TALKING. IF YOU LOOK AT THE LAST SENTENCE OF WHAT I HAVE HIGHLIGHTED HERE, BECAUSE OF THE PROBLEMS WITH SPONTANEOUS ADVERSE EVENTS, THE FDA MUST RELY ON ADEQUATELY POWERED, RANDOMIZED, CONTROLLED TRIALS OR WELL-DESIGNED OBSERVATIONAL STUDIES TO DETERMINE IF COMMON EVENTS IN THE RECIPIENT POPULATION CAN BE ATTRIBUTED, LIKE IN THIS CASE, TO VICTOZA EXPOSURE.

THE OTHER THING IS IF YOU THINK ABOUT THE OTHER SIDE OF THE SPECTRUM, WHEN YOU ARE TALKING ABOUT SOMETHING THAT REALLY DOESN'T HAPPEN IN THE BACKGROUND POPULATION ABSENT A DRUG EXPOSURE -- LIKE, YOU SEE A LOT OF CASES WITH STEVENS JOHNSON SYNDROME AND THINGS LIKE THAT -- IF THEY DON'T HAPPEN, IT IS MORE INFORMATIVE AND MAY ALLOW FOR AN INFERENCE IF YOU HAVE ENOUGH OF THOSE KINDS OF CASES.

AND PROBABLY ACUTE PANCREATITIS MAY NOT BE AS GOOD OF

AN EXAMPLE AS AN ACUTE SKIN REACTION, WHERE SOMETHING LIKE THAT GENERALLY DOESN'T HAPPEN IN THE ABSENCE OF A DRUG EXPOSURE. AN ACUTE INJURY, LIKE ACUTE PANCREATITIS, IN CLOSE PROXIMITY TO DRUG EXPOSURE MAY BE MORE INFORMATIVE THAN A PANCREATIC CANCER DIAGNOSES IN RELATION TO DRUG THERAPY. AND THE AGENCY RECOGNIZES THAT.

YOU ALSO HAVE MULTIPLE OTHER PROBLEMS. WE GOT INTO THIS AT SCIENCE DAY WITH USING ADVERSE EVENT REPORTS. THEY ARE ONLY REPORTS. THEY ARE NOT WHAT REALLY HAPPENED. SO YOU CAN'T CALCULATE THE RISK OF THE EVENT IN THE PATIENTS TAKING IT COMPARED TO THE ACTUAL RISK OF THE EVENT IN SIMILAR PATIENTS NOT TAKING IT, WITHOUT A CONTROLLED STUDY.

AND THAT'S WHY THE FDA HAS CLEARLY DISTINGUISHED PANCREATITIS FROM PANCREATIC CANCER IN THIS CONTEXT AND SAID IT TWICE, QUITE CONCLUSIVELY. IN FACT, AGAIN, IN THE RESPONSE TO THE CITIZEN'S PETITION -- AND IF YOU LOOK HERE, THEY GO FURTHER BECAUSE WE DON'T HAVE TO SPECULATE ABOUT WHETHER OR NOT THEY WOULD REJECT A WARNING BASED ON SPONTANEOUS ADVERSE EVENT REPORTS. THEY ACTUALLY ADDRESS THAT QUESTION. THEY LOOKED AT SPONTANEOUS ADVERSE EVENT REPORTS. AND IN THE FIRST SENTENCE OF THE SECOND PARAGRAPH, YOU CAN SEE IN THEIR OWN REVIEW OF 49 UNIQUE CASES, TAKEN FROM THE RELEVANT AE DATABASE, WE FOUND NO EVIDENCE REGARDING THE RISK OF PANCREATIC CARCINOMA IN ASSOCIATION WITH THE USE OF VICTOZA THAT WOULD SUPPORT ANY CHANGES TO THE CURRENT APPROVED LABELING.

THEY HAVE ACTUALLY AFFIRMATIVELY REJECTED THE IDEA THAT AES SHOULD OR COULD BE PART OF LABELING POST-APPROVAL. SO THERE IS NO SPECULATION AT ALL.

AND THE LAST POINT I WOULD MAKE IS MR. BOGRAD SAID THAT -- HE SAID THIS A COUPLE OF TIMES -- WE DON'T KNOW HOW THE AGENCY WOULD RESPOND TO A PROPERLY SUPPORTED CBE. WE DON'T KNOW HOW THEY WOULD DO THAT.

AND JUST FOCUSING ON THE RECORD THAT WE HAVE IN FRONT OF US, AND WHAT WE KNOW THE FDA DID REVIEW, THE REGS DEFINE, AS MR. HEARD SAID, WHAT IS PROPER SUPPORT FOR A CBE. AND THEY DEFINE THAT, AS MR. HEARD SAID, AS REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION.

WE KNOW, BASED ON THE RECORD THAT THE FDA REVIEWED, THAT IT IS EXPLICITLY FOUND THERE IS NO REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION.

THE QUOTE THAT HE JUST SHOWED YOU -- AND THAT I SHOWED YOU AGAIN -- YOU CAN'T READ THE SENTENCE THAT SAYS, THEREFORE, ANY SUSPICION OF A CAUSAL ASSOCIATION BETWEEN EXPOSURE TO VICTOZA AND PANCREATIC CANCER IS INDETERMINATE AT THIS TIME, AND CONCLUDE -- REASONABLY CONCLUDE THAT THEY WOULD ALLOW A PANCREATIC CANCER WARNING IN THE FACE OF THE EVIDENCE THEY REVIEWED.

YOU CAN'T DO THAT. THIS SAYS "ANY SUSPICION." SO WHAT THE PLAINTIFFS ARE ASKING YOUR HONORS TO DO IS TO DENY A MOTION ON THE POSSIBILITY THAT FDA WOULD ACCEPT A CBE THAT

VIOLATES ITS OWN STANDARD. THAT IS WHAT THEY ARE ASKING YOU TO DO.

WE BELIEVE THAT THE FACT THAT THE FDA HAS EXPLICITLY FOUND NO EVIDENCE TO SUPPORT EVEN A SUSPICION OF CAUSALITY IS VERY CLEAR EVIDENCE THAT IT WOULD NOT ACCEPT A CBE THAT DOESN'T SATISFY ITS OWN STANDARD. THANK YOU, YOUR HONORS.

THE COURT: OKAY. THANK YOU. PLAINTIFFS, YOUR FINAL COMMENTS. MR. BOGRAD, ARE YOU TAKING THE HELM AGAIN?

MR. BOGRAD: NOT REALLY, YOUR HONOR. I AM GOING TO SAY VERY LITTLE. I BELIEVE MY COLLEAGUES FROM THE JCCP WOULD LIKE TO MAKE A FEW REMARKS. BUT THE ONLY REASON WE EVEN HAVE THIS SURREBUTTAL IS BECAUSE OF OUR -- THEORETICALLY -- IS BECAUSE OF OUR AFFIRMATIVE MOTION. I FEEL LIKE I HAVE ALREADY ADDRESSED THAT ISSUE.

I DIDN'T HEAR ANYTHING NEW IN THE DEFENDANTS' REPLY. THEY CONTINUE TO SAY THAT THEY DISAGREE WITH MY UNDERSTANDING OF THE LAW. THEY DISAGREE WITH WHAT THE SUPREME COURT SAID IN *WYETH V. LEVINE.* THEY THINK THAT AS LONG AS THE FDA DOESN'T MANDATE A WARNING, THEY WIN. AND WE DISAGREE.

AND I AM HAPPY TO ANSWER SPECIFIC QUESTIONS FROM THE BENCH, BUT I DIDN'T HEAR ANYTHING NEW HERE.

I DO THINK IT'S IMPORTANT TO REMEMBER THAT THE FDA FILINGS IN THE EGAN STUDY IS THAT A CORRELATION HAS NOT BEEN DEFINITIVELY -- A CAUSAL RELATION HAS NOT BEEN DEFINITIVELY -- THEY HAVE REACHED NO FINAL CONCLUSION.

THAT IS NOT THE SAME THING AS SAYING THAT THERE IS NO REASONABLE EVIDENCE. AND I THINK THE QUESTION REMAINS SPECULATIVE ABOUT WHAT THEY WOULD HAVE DONE.

THE COURT: IS THERE EVER A FINAL CONCLUSION IN SCIENCE?

MR. BOGRAD: WELL, NOT IN SCIENCE, YOUR HONOR. BUT THERE IS OFTEN A FINAL CONCLUSION IN A CLEAR EVIDENCE ANALYSIS. IT OCCURS WHEN THE DEFENDANTS SUBMIT A CBE OR A PRIOR APPROVAL SUPPLEMENT TO ADD A WARNING BASED UPON THE EVIDENCE THAT THE PLAINTIFFS CLAIM SHOULD HAVE LED TO WARNING, AND THE FDA SAYS NO. THAT IS FINAL CONCLUSIVE EVIDENCE.

AND, YOU KNOW, THE DEFENDANTS THINK THAT THEY HAVE GOT SOME PROXY FOR THAT, BUT ALL THE CASES THAT HAVE HELD CLEAR EVIDENCE HAVE REQUIRED MORE THAN THAT. AND WE THINK THEY HAVEN'T MET THEIR BURDEN; AND, THEREFORE, THEIR MOTION SHOULD BE DENIED.

BUT I WOULD LIKE TO TURN THE FLOOR TO MY COLLEAGUES FROM THE JCCP.

THE COURT: LET ME POSE TWO QUESTIONS THAT YOU CAN DEFER OR ADDRESS OR BOTH. THE DEFENSE HAS TAKEN AN APPROACH WHERE THEY HAVE LISTED SEVEN THINGS VERY SUCCINCTLY THAT ESTABLISH CLEAR EVIDENCE.

IF YOU WERE TO CREATE A SIMILAR LIST THAT WOULD REFUTE THEIR EVIDENCE, WHAT WOULD IT CONTAIN?

THE SECOND QUESTION IS WE DON'T KNOW WHAT THE FDA

CONSIDERED IN TOTAL. I DON'T THINK ANYBODY EVER KNOWS THAT. GIVEN JUST THE CONSTRUCT OF THAT, HOW IS A DEFENDANT EVER GOING TO ESTABLISH CLEAR EVIDENCE, OR THE PLAINTIFF TRULY CHALLENGE, IF WE TAKE IT AS A GIVEN THAT WE ARE NEVER GOING THERE, AND WE ULTIMATELY FALL BACK ON WHAT IS THE AVAILABLE SCIENCE AT THE GIVEN TIME WHERE THE DECISION IS FOCUSED?

MR. BOGRAD: WELL, LET ME START WITH THAT SECOND QUESTION, YOUR HONOR. AND I WOULD LIKE TO GO BACK TO MY REMARKS EARLIER. THE ONLY THING WE ARE DEBATING RIGHT HERE IS IMPOSSIBILITY PREEMPTION AND WHETHER IT WOULD HAVE BEEN IMPOSSIBLE FOR THEM TO PROVIDE A WARNING. THAT IS NOT THE ULTIMATE QUESTION IN THE LITIGATION, AND THAT QUESTION IS ONE WHERE THERE WILL BE FIGHTS ABOUT FACT.

BUT IN ORDER TO ESTABLISH IMPOSSIBILITY, YOU NEED A CLEAR ANSWER ABOUT WHAT THE FDA WOULD HAVE DONE. I HAVE SUGGESTED THAT THERE ARE SEVERAL WAYS IN WHICH WE CAN GET A CLEAR ANSWER WITH WHAT THE FDA WOULD HAVE DONE. YOU CAN GO TO THE FDA WITH CBE REQUEST AND SEE IF THE FDA SAYS NO. YOU CAN GO TO THE FDA WITH A PRIOR APPROVAL SUPPLEMENT AND SEE IF THE FDA SAYS NO. YOU CAN CONTACT THE FDA, SAY HERE IS ALL THIS INFORMATION WE HAVE, WE ARE CONCERNED THAT PERHAPS A WARNING SHOULD BE REQUIRED, AND THE FDA MIGHT RESPOND BY SAYING WE'VE CONSIDERED ALL THIS EVIDENCE, AND NO.

YOU KNOW, THE FDA COULD HAVE ORDERED THE ADDITION OF A STATEMENT TO LABELING ON THE BASIS OF EGAN, WHERE THEY SAID

WE REQUIRE THE DEFENDANTS TO ADD A STATEMENT REFUTING THE NOTION THAT THERE IS A PANCREATIC CANCER RISK HERE.

THAT DOESN'T MEAN THAT THE SCIENCE IS DEFINITIVE, BUT THERE ARE WAYS TO KNOW, TO HAVE CLEAR EVIDENCE WHAT THE FDA WOULD HAVE DONE.

THE COURT: BRING IT BACK TO THE SCIENCE, THEN. WHAT SCIENTIFIC HALLMARKS ARE THERE TO BASICALLY DISPUTE THIS CONCEPT OF CLEAR EVIDENCE, OR TO RAISE SUFFICIENT DOUBT, HOWEVER WE CHARACTERIZE THAT, SUCH THAT IT DEFEATS THE CLEAR EVIDENCE BURDEN THAT THE DEFENSE HAS?

MR. BOGRAD: LET ME GIVE YOU --

THE COURT: GIVE ME THE BULLET LIST.

MR. BOGRAD: I AM GOING TO DO THAT, YOUR HONOR.

THE COURT: GIVE ME THE BULLET LIST.

MR. BOGRAD: LET ME GIVE YOU SEVERAL PIECES. THE FIRST BULLET POINT IS THAT ALL OF THE EVIDENCE THAT THE DEFENDANTS CITE TO IS EVIDENCE ABOUT THE QUESTION WHETHER THE FDA BELIEVES THERE IS SUFFICIENT SCIENCE TO MANDATE A WARNING.

AND WHILE DEFENDANTS SAY THERE IS NO DIFFERENCE, THE FACT IS THE ONLY STANDARD THAT HAS TO BE MET IN ORDER TO PUT A WARNING ON THE LABEL IS REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION. AND, INDEED, 201.57(C)(6) SPECIFICALLY SAYS, YOU KNOW, A CAUSAL ASSOCIATION NEED NOT HAVE BEEN DEFINITIVELY ESTABLISHED.

THE COURT: SO GO TO THE REASONABLE STANDARD. GIVE

ME THE DATA POINTS THAT WOULD SUPPORT A REASONABLE FINDING AT THIS POINT, OF A CONNECTION BETWEEN THE MEDICATION AND PANCREATIC CANCER.

MR. BOGRAD: WELL, YOUR HONOR, JUST TO MAKE IT VERY SIMPLE.

THE COURT: AND NOT ANY OF THIS BUSINESS ABOUT THEY DIDN'T ASK FOR A CBE OR THEY DIDN'T SUPPLY THIS. NOT WHAT THEY DID. WE'RE TALKING SCIENCE. WHAT IS THE DATA THAT WOULD SUPPORT THE FDA COMING TO A CONCLUSION THAT THERE IS A REASONABLE CONNECTION BETWEEN THE DRUGS AND PANCREATIC CANCER THAT WOULD ALLOW A WARNING.

MR. BOGRAD: WELL, YOUR HONOR, I REFER YOU TO HEALTH CANADA AND TO THE FIVE-PAGE SUMMARY THAT I MENTIONED BEFORE. I THINK IT'S PAGES 46 TO 50 OF HEALTH CANADA. HEALTH CANADA DID A COMPREHENSIVE SIGNAL ASSESSMENT -- JUST LIKE THE DEFENDANTS SAY THE FDA DID -- REVIEWED A WIDE VARIETY OF SCIENTIFIC DATA AND CONCLUDED THAT THAT DATA WAS SUFFICIENT. THEIR LEGAL STANDARD MAY NOT BE REASONABLE EVIDENCE OF CAUSAL ASSOCIATION.

THE COURT: THAT'S RIGHT. IN THEIR REGULATORY SCHEME, THEY DO SOMETHING THEY WANTED, A WARNING, GIVEN THE EVIDENCE THEY HAD.

MR. BOGRAD: YES.

JUDGE HIGHBERGER: BUT UNDER A DIFFERENT STANDARD.

MR. BOGRAD: YES, YOUR HONOR. I'M NOT TALKING ABOUT THEIR BOTTOM LINE. THEY LAY OUT IN LABORIOUS DETAIL 98 PAGES

OF SCIENTIFIC FINDINGS THAT LED THEM TO THE CONCLUSION. AND I DON'T KNOW WHAT THE LEGAL STANDARD FOR ADDING A WARNING IS IN CANADA, BUT I'M PRETTY CERTAIN IT'S NOT YOU CAN PUT A WARNING ON EVEN IF THERE IS NO SCIENCE TO SUPPORT IT.

THE COURT: I HOPE NOT.

MR. BOGRAD: RIGHT. SO WE HAVE TO ASSUME THAT WHETHER THE PHRASE IS REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION OR NOT, THAT THERE WAS EVIDENCE THERE THAT THEY THOUGHT WAS SUFFICIENT.

AS I SAID EARLIER, THE FDA ALSO TAKES INTO ACCOUNT THE VIEWS OF THE MANUFACTURER. AND IF THE MANUFACTURER BELIEVES THAT THERE IS A REASON TO ADD A WARNING, THE FDA WILL TAKE THAT INTO ACCOUNT. THAT IS ANOTHER FACTOR THAT WAS NOT BEFORE THE FDA IN THE CONTEXT OF THE EGAN ANALYSIS.

AND THEN THERE IS ALL THIS NEW EVIDENCE, THE OTHER PIECES OF NEW EVIDENCE WE HAVE IDENTIFIED IN THE RECORD. NEW SAFETY INFORMATION THAT WE THINK ADDED TO THE WEALTH OF INFORMATION THAT THEY ALREADY HAD, WHICH PUSHES THE EQUATION OVER THE EDGE.

THE COURT: WHILE IT'S NOT DISPOSITIVE, IT'S PROBABLY INFORMATIVE TO THE DISCUSSION THAT THERE HAVE BEEN FOUR ADDITIONAL MEDICATIONS APPROVED WITHOUT WARNINGS IN THE FACE OF HEALTH CANADA AND EVERYTHING ELSE.

MR. BOGRAD: WELL, IT'S NOT IN THE FACE OF HEALTH CANADA, YOUR HONOR, BECAUSE WE HAVE NO WAY OF KNOWING IF THE

FDA WAS AWARE OF HEALTH CANADA.

THE COURT: MERCK KNOWS IT'S OUT THERE, RIGHT?

MR. BOGRAD: MERCK KNOWS IT'S OUT THERE.

THE COURT: APPARENTLY YOU GUYS KNOW IT'S OUT THERE.

MR. GOETZ: WE ONLY KNOW IT'S OUT THERE FROM DISCOVERY, YOUR HONOR.

THE COURT: YOUR CODEFENDANTS KNOW IT'S OUT THERE, YET THERE IS MORE DRUGS GOING IN. AND IS THIS INFORMATION BEING SUPPRESSED FROM THE FDA? THESE DEFENDANTS ARE ENGAGED IN SOME SORT OF MASSIVE FRAUD ON THE FDA BEYOND THE ISSUES IN *BUCKMAN*, AN OUTRIGHT FRAUD ON THE PUBLIC?

MR. GOETZ: YOUR HONOR, WE DON'T KNOW WHETHER THE FDA HAS HEALTH CANADA. THERE IS CERTAINLY NO REFERENCE TO IT IN ANY OF THESE MATERIALS THAT THEY ARE TALKING ABOUT. SO I AM NOT MAKING ANY REPRESENTATION THAT THEY HAVE ENGAGED IN FRAUD ON THE FDA OR ON THE PUBLIC. I'M SAYING THERE IS SUFFICIENT EVIDENCE, NEW SAFETY INFORMATION, TO SUPPORT REASONABLE EVIDENCE OF A CAUSAL ASSOCIATION THAT WOULD JUSTIFY A WARNING.

AND THAT WARNING, THAT COULD HAVE CERTAINLY BEEN A QUALIFIED WARNING. IT COULD CERTAINLY HAVE EXPRESSED SOME OF THE LIMITATIONS IN THE DATA. BUT GIVEN WHAT PEOPLE KNEW, GIVEN THE SPONTANEOUS REPORTS, GIVEN THE CLINICAL TRIAL IMBALANCES, GIVEN THE CLEAR METHOD BIOLOGICAL PLAUSIBILITY, GIVEN THE CLINICAL AND NONCLINICAL ASSESSMENTS, WE THINK THAT WE WILL ULTIMATELY BE ABLE TO SHOW THAT THERE WAS A REASONABLE BASIS TO

ADD A WARNING, AND THAT DOCTORS WOULD HAVE WANTED TO HAVE BEEN INFORMED. AND THEN THEIR FAILURE TO BE INFORMED HAS CAUSED INJURIES TO A NUMBER OF THESE PLAINTIFFS.

THE COURT: OKAY.

MR. BOGRAD: AND WITH THAT I WILL CEDE THE FLOOR TO MY COLLEAGUES FROM THE JCCP.

THE COURT: FOLKS.

MR. DEPEW: I'D LIKE TO RESPOND DIRECTLY TO YOUR QUESTIONS, YOUR HONOR, IF I MAY. I BELIEVE THAT YOU ASKED FOR SOME DATA POINTS. WE PROVIDED JUDGE HIGHBERGER A BINDER WITH A LIST OF THE SCIENTIFIC MATERIAL, BUT I WILL SUMMARIZE IT FOR YOU NOW. LET'S START WITH ELASHOFF.

JUDGE HIGHBERGER: WHAT BINDER, WHEN?

MS. CROOKE: IT WAS OUR EXHIBITS, YOUR HONOR.

JUDGE HIGHBERGER: I HAVE EXHIBITS, BUT NOT A BINDER. I HAVE THIS STUFF.

MS. CROOKE: WE DIDN'T BINDER IT. IT WAS THE EXHIBITS TO THE OPPOSITION TO THE DECLARATIONS.

JUDGE HIGHBERGER: SO I HAVE THE DEPEW DECLARATION AND EXHIBITS?

MS. CROOKE: CORRECT.

JUDGE HIGHBERGER: OKAY. THAT IS YOUR BINDER.

MS. CROOKE: 1 THROUGH 49.

JUDGE HIGHBERGER: COME AGAIN?

MS. CROOKE: 1 THROUGH 49.

JUDGE HIGHBERGER: CONTINUE.

THE COURT: GO AHEAD, MR. DEPEW.

MR. DEPEW: BUT WHAT I WANT TO DO IS I'M GOING TO HIT THE HIGHLIGHTS. I'M NOT GOING TO GO THROUGH EVERY JOURNAL ARTICLE, BUT I'M GOING TO GIVE YOU THE NAME OF THE LEAD AUTHOR AND WHAT THE SIGNIFICANCE IS.

THE FIRST IMPORTANT ONE IS THE ELASHOFF STUDY, WHICH IS A FAERS DATABASE ANALYSIS, WHICH FOUND THAT THERE WAS A STATISTICALLY SIGNIFICANT INCREASE IN THE RECORDING RATE OF PANCREATIC CANCER AMONG THESE DRUGS. THAT STUDY WAS INDEPENDENTLY CONFIRMED BY THE NAUCK STUDY, N-A-U-C-K.

THE COURT: N-A-U-

MR. DEPEW: N-A-U-C-K. THOSE TWO STUDIES WERE FURTHER INDEPENDENTLY CONFIRMED BY THE FENG STUDY. THESE ARE ALL ADVERSE EVENT REPORTING DATABASE ANALYSES THAT WERE STATISTICALLY SIGNIFICANT IN TERMS OF THE DISPROPORTIONALITY FOR REPORTING FOR PANCREATIC CANCER.

THERE WERE OBSERVATIONAL STUDIES THAT WERE ALSO DONE. THE FIRST ONE I WOULD LIKE TO DRAW YOUR ATTENTION TO, AND YOU CAN READ THIS, IS THE ROMLEY STUDY. AND IF YOU GO TO THE SECTION WHERE THERE IS A CHART WHERE THEY TALK ABOUT PANCREATIC CANCER, YOU CAN SEE THAT THEY IDENTIFY A NONSIGNIFICANT BUT POSITIVE ASSOCIATION BETWEEN THESE DRUGS AND PANCREATIC CANCER.

JUDGE HIGHBERGER: WHICH EXHIBIT NUMBER?

MS. CROOKE: I DON'T BELIEVE ROMLEY WAS SPECIFIC TO

DR. CARSON'S REPORT, WHICH IS AN EXHIBIT. DR. CARSON DISCUSSED THAT AND SOME OF THE OTHERS AT LENGTH.

JUDGE HIGHBERGER: WELL, I'M TRYING TO FIND IT IN THE RECORD. WHAT EXHIBIT DID THE DEPEW DECLARATION PROVIDE AS A BASIS FOR THIS ARGUMENT?

MS. CROOKE: ROMLEY IS NOT ATTACHED.

MR. DEPEW: I THOUGHT ROMLEY WAS. IF YOU COULD GIVE ME CARSON.

MS. CROOKE: EXHIBIT 30, DR. CARSON'S REPORT.

JUDGE HIGHBERGER: THREE-ZERO?

MS. CROOKE: THREE-ZERO.

JUDGE HIGHBERGER: SO DR. CARSON'S REPORT TALKS ABOUT THIS?

MR. DEPEW: CORRECT.

JUDGE HIGHBERGER: IS THIS CHART PART OF CARSON'S REPORT?

MS. CROOKE: I DON'T BELIEVE SO.

JUDGE HIGHBERGER: SO THE CHART IS NOT BEFORE THE COURT?

MR. DEPEW: I THINK THAT THE STATISTIC I JUST REFERRED TO IS EXTRACTED FROM THE REPORT, BUT I CAN SUPPLY THE CHART. BUT THE STATISTIC THAT I JUST DESCRIBED IS IN THE CARSON REPORT.

AND LASTLY -- AND THIS MAY BE TRUE FOR -- THE LAST ONE -- I KNOW IT'S DISCUSSED IN THE CARSON REPORT -- IS CHANG.

THAT WAS AN OBSERVATIONAL STUDY BASED UPON THE TAIWANESE NATIONAL HEALTHCARE SYSTEM, PROBABLY THE LARGEST OF ALL OF THESE STUDIES IN TERMS OF THE NUMBER OF PARTICIPANTS THAT WERE EVALUATED. THIS WAS AN OBSERVATIONAL STUDY THAT WAS STATISTICALLY SIGNIFICANT FOR PANCREATIC CANCER. IT SHOWED A DOUBLING OF THE RISK. THAT IS IN TABLE ONE. AND THAT IS ALSO DISCUSSED IN THE CARSON REPORT.

SO IN TERMS OF HUMAN DATA, THOSE ARE ALL POSITIVE ASSOCIATIONS TAKEN FROM HUMAN DATA FOR PANCREATIC CANCER.

JUDGE HIGHBERGER: DID ANY OF THE ANIMAL STUDIES OBSERVE PANCREATIC CANCER IN THE SUBJECTS, AS OPPOSED TO OTHER ABNORMALITIES?

MR. DEPEW: I'M SORRY. I DIDN'T FOLLOW.

JUDGE HIGHBERGER: DID ANY OF THE ANIMAL STUDIES, TO YOUR UNDERSTANDING, SHOW EVIDENCE OF PANCREATIC CANCER AS SUCH IN THE ANIMALS, AS COMPARED TO OTHER VARIETIES OF ABNORMALITIES?

MR. DEPEW: WHAT THE ANIMAL STUDIES SHOW -- AND IT'S ACTUALLY A CONTINUUM OF THE PANIN LESIONS, WHICH ARE THESE PRECURSOR LESIONS THAT RESIDE IN THE PANCREAS. AND SO WHAT WE HAVE ARE AN ENTIRE SERIES OF STUDIES LEADING UP TO THE TWO MOST IMPORTANT, WHICH IS THE GIER STUDY, WHICH WAS PUBLISHED IN 2012, EXHIBIT 19.

THE GIER STUDY ADDRESSES THE ISSUE OF LOOKING AT BOTH MICE AND RATS, AS WELL AS HUMAN PANCREATIC CELLS, IDENTIFIED

THE MECHANISM BY WHICH THESE DRUGS CAUSE CELL PROLIFERATION, AND IDENTIFIED IT ON PANINS 1, 2, AND 3, SHOWING THAT THESE CELLS ALL RESPONDED TO ACCELERATED CELL PROLIFERATION IN THE ANIMAL MODEL, WHICH IS THE VERY MECHANISM OF ACTION THAT IS THE BASIS OF THIS CASE.

JUDGE HIGHBERGER: IS THAT, IN NON-TECHNICAL TERMS, AN OBSERVATION BY DR. GIER OF PRECANCEROUS CONDITIONS AS OPPOSED TO FULL-ON CANCER?

MR. DEPEW: WELL, THE OBSERVATION OF CANCER IN ANIMALS IS A DIFFICULT OBSERVATION, TYPICALLY, BECAUSE THESE ANIMALS ARE SACRIFICED AT AN EARLY STAGE IN THE PERIOD.

IF YOU GO BACK AND LOOK AT ALL OF THESE STUDIES, THE ANIMAL STUDIES DATE BACK TO 1999 AND THEN 2000 ARE THE EARLIEST ANIMAL STUDIES THAT LOOK AT THIS PROLIFERATION PHENOMENON. AND TYPICALLY THEY USE JUVENILES. THEY ARE WEEKS OLD AND THEY GIVE THEM THESE DOSES AND SACRIFICE THEM EARLY.

SO THE ONLY ANIMAL MODEL THAT COMES CLOSE TO REPLICATING WHAT WOULD BE A CANCER MODEL IS THE GIER STUDY, WHERE THEY TOOK THESE MICE AND THEY GENETICALLY ENGINEERED THEM SO THEY ALREADY HAD CERTAIN GENETIC MODIFICATIONS, THE KRAS GENE MUTATION, WHICH WAS THE SETUP FOR THE CANCER.

THIS WAS IMPORTANT BECAUSE I THINK IT GETS TO A CONCERN THAT YOU HAVE, JUDGE BATTAGLIA, ABOUT LATENCY AND WHAT WE COMMONLY HEAR ABOUT THIS INTERVAL FROM EXPOSURE TO THE TIME OF DIAGNOSES.

ALL OF THE EVIDENCE THAT HAS BEEN PRESENTED BY THE DEFENDANTS REGARDING THAT IS THEY ARE TALKING ABOUT THE INITIAL GENETIC EVENT, THE ONCOGENIC EVENT IN THAT TIME INTERVAL. THAT IS NOT THIS CASE.

IF YOU REMEMBER CORRECTLY, WHEN WE WERE LOOKING BACK AT SCIENCE DAY, WE WERE NOT TALKING ABOUT YOUNG, HEALTHY PEOPLE WHO DON'T HAVE THESE PRECURSOR LESIONS WHO PRIME THEM FOR THESE CANCERS. THESE ARE TYPICALLY PEOPLE IN THEIR 50S AND 60S. IN FACT, THE MOST COMMON AGE FOR THE ONSET OF TYPE II DIABETES OCCURS BETWEEN THE AGE OF 50 AND 60.

BETWEEN THE AGE OF 50 AND 60, 70 PERCENT OF US HAVE PRECURSOR LESIONS IN OUR PANCREAS. SO YOU ARE PRIMED ALREADY WITH A SEQUENCE OF MUTATIONS THAT PUSHES YOU OVER THE CLIFF. SO THE TYPICAL MODEL FOR LATENCY -- IN OTHER WORDS, THE FIRST ONCOGENIC EVENT TO DIAGNOSIS, LIKE IN THE RADIATION EXPOSURE CASES, WHERE YOU KNOW WHEN THE EVENT OCCURRED, THE ATOMIC BOMB SURVIVORS, TO WHEN THEY STARTED SEEING CANCERS. THE MOST RECENT REPORT PUBLISHED IN 2005 HAS THE AVERAGE LATENCY PERIOD FOR THAT OF FIVE YEARS. THAT IS NOT THIS CASE.

OUR CASES ARE A SUBSET OF PEOPLE WHO ARE ALREADY PRIMED WITH PREMALIGNANT LESIONS AND THEY ARE PUSHED OVER THE EDGE, WHICH IS WHY YOU GET THIS SHORTER LATENCY PERIOD. AND THERE IS EVIDENCE WHERE THEY HAVE ACTUALLY TRIED TO PICK UP WITH -- IT'S IN THE LITERATURE, TOO, WHERE THEY DO CT SCANS OF PEOPLE WITH PERFECTLY NORMAL PANCREASES AND THEN THEY ARE

SUBSEQUENTLY DIAGNOSED WITH PANCREATIC CANCER. AND THEY TRIED TO IDENTIFY WHAT THAT INTERVAL IS. AND IT'S AS SHORT AS FOUR MONTHS.

SO THAT'S WHAT HAPPENS WHEN YOU HAVE SOMEBODY THAT IS ALREADY ALONG THE LINE. SO IN TERMS OF DATA POINTS, IT'S THOSE STUDIES ON HUMAN DATA.

AND THEN, I BELIEVE -- IS THE MARKED EXPANSION IN OUR LIST?

MS. CROOKE: THAT IS 26.

MR. DEPEW: 26. THIS IS THE RESEARCHERS. THERE IS A GROUP OF RESEARCHERS OUT OF UCLA. THEY ACTUALLY HAVE THEIR OWN LABORATORY BUILDING DEVOTED TO THE RESEARCH OF DISEASES OF THE PANCREAS. AND I BELIEVE THE LEAD AUTHOR IS ALEXANDER BUTLER. THIS IS WHERE THEY ACTUALLY TOOK ORGANS FROM HUMAN ORGAN DONORS THAT WERE DIABETIC, NOT ON THESE DRUGS, AND DIABETICS ON THESE DRUGS. THESE PEOPLE DIED FOR OTHER REASONS, BUT THEY DONATED THEIR ORGANS.

AND THE RESEARCHERS AT UCLA, IN CONNECTION WITH -- WORKING IN CONJUNCTION WITH RESEARCHERS AT THE UNIVERSITY OF MIAMI, DID PATHOLOGICAL COMPARATIVE STUDIES. AND THEY LOOKED AT THE SIZE, THE WEIGHT, AND THE FREQUENCY OF THE LESIONS IN HUMANS. AND THEY DETERMINED -- THEY DID A STATISTICAL ANALYSIS AND FOUND THAT THEY WERE, ON AVERAGE, LARGER, MEANING THE CELLS WERE PROLIFERATING IN THESE HUMANS. SO THERE WAS HUMAN DATA. AND THEY FOUND THAT THERE WAS A SIGNIFICANT INCREASE IN THE

LESIONS AT THE HEAD OF THE PANCREAS, AMONG THESE HUMAN SUBJECTS. SO THERE IS HUMAN DATA THERE.

SO THE CONTINUUM IS THE DATA GOING BACK FOR -- AS EARLY AS 2000 WHEN THEY STARTED LOOKING AT THESE YOUNG JUVENILE ANIMALS THAT TYPICALLY DON'T GET CANCER BECAUSE THEY ARE SACRIFICED EARLY, TO THE GIER STUDY, WHERE THEY ARE NOW TINKERING WITH THE MODEL OF THE MIDDLE-AGED ADULT THAT HAS THESE PRECURSOR LESIONS, AND FOUND THAT THEY COULD CONVERT THEM. AND THEY WERE GENERATING PROLIFERATION IN THESE PRECURSOR LESIONS -- PANINS 1S, 2S AND 3S.

WHEN YOU ARE AT A PANIN 3, YOU ARE LITERALLY ON THE EDGE OF CANCER. IT'S AS CLOSE TO GETTING CANCER AS YOU CAN GET WITHOUT HAVING A DIAGNOSIS OF PURE CANCER, A MALIGNANCY. AND THEY IDENTIFIED THIS IN BOTH THE ANIMAL AND THE HUMAN. SO THAT IS THE SUMMARY OF THE DATA POINTS.

WHAT WE DON'T KNOW ABOUT IN THE EGAN LETTER IS THEY SAY THEY DID A COMPREHENSIVE REVIEW, BUT WE DON'T KNOW WHAT METHODOLOGY THEY APPLIED TO THE REVIEW. WE DON'T KNOW IF THIS WAS A WEIGHT-OF-EVIDENCE METHODOLOGY. HOW DID THEY WEIGHT THE CONFLICTING DATA? HOW DID THEY RESOLVE THE INCONSISTENCIES?

IN FACT, EGAN, IN THAT LETTER, ACKNOWLEDGES THAT THERE IS EVIDENCE THAT IS INCONSISTENT WITH THEIR RESULT. IT'S A BLACK BOX. WE DON'T KNOW AND WILL NEVER KNOW HOW THEY RESOLVED THIS, SO WE ARE LEFT TO SPECULATE HOW THEY WEIGHED IT.

BUT WHAT WE DO KNOW IS THAT WHEN THEY LOOKED AT THIS,

THEY WERE LOOKING AT THIS IN THE CONTEXT OF WHETHER OR NOT THESE DRUGS ACTED AS A MUTAGEN, NOT A CELL PROLIFERATOR.

OUR CASE HAS ALWAYS BEEN THAT THEY ARE NOT MUTAGENIC. AND IF YOU GO BACK TO SCIENCE DAY AND IF YOU LOOK AT THAT HANDOUT THAT I GAVE YOU, OUR POSITION WAS THAT THESE DRUGS ARE NOT MUTAGENIC. THEY DON'T DIRECTLY CAUSE MUTATIONS. WHAT THEY DO IS THEY CAUSE CELL PROLIFERATION THAT INCREASES THE ACCUMULATION OF MUTATIONS ONCE THEY OCCUR. IT ACCELERATES THE PROCESS.

SO, THEREFORE, IT'S WHAT'S CALLED A NON-MUTAGENETIC CARCINOGEN, JUST LIKE ESTROGEN. ESTROGEN IS A DRUG THAT IS LISTED BY THE NTP, THE NATIONAL TOXICOLOGY PROGRAM, AS A HUMAN CARCINOGEN. IT IS A NATURALLY OCCURRING HORMONE.

THE CALIFORNIA COMMITTEE ON CANCER IDENTIFICATION LISTS ESTROGEN AS A HUMAN CARCINOGEN. IT IS NOT A MUTAGEN. IT CAUSES CELL PROLIFERATION, WHICH IS WHY ESTROGEN IS TYPICALLY USED FOR YOUNG WOMEN SAFELY AS A BIRTH CONTROL. BUT MIDDLE-AGED WOMEN WHO ARE MENOPAUSAL AND HAVE PRECURSOR LESIONS IN THEIR BREASTS ARE AT RISK FOR GETTING BREAST CANCER, WHICH IS WHY DOCTORS TYPICALLY DON'T GIVE ESTROGEN FOR HORMONE REPLACEMENT THERAPY TO MIDDLE-AGED WOMEN.

THAT IS OUR CASE, A SUBSET OF PEOPLE WHO ARE MIDDLE-AGED, WHO ARE PRIMED FOR THIS DISEASE, WHO HAVE ACCUMULATED ALREADY, IN THEIR MIDDLE AGE, THESE MUTATIONS, THEY GET STARTED ON THESE DRUGS TYPICALLY BETWEEN THE AGE OF 50 AND

60, AND IT ACCELERATES THE PROCESS.

IF YOU GAVE THIS DRUG TO A 17-YEAR-OLD CHEERLEADER THEY WILL NEVER GET PANCREATIC CANCER BECAUSE THEY DON'T FIT THAT MODEL OF BEING PRIMED. SO THAT IS A BASIC SUMMARY OF OUR DATA POINTS.

ONE LAST COMMENT, AND I WILL SIT DOWN. I BELIEVE, JUDGE BATTAGLIA, YOU HAD SOME CONCERNS ABOUT THE UTILITY OF THE SPONTANEOUS REPORTING DATABASE THAT IS USED. AND SOMEONE ONCE SAID -- I FORGET WHO IT WAS -- THAT HISTORY IS PROLOGUE.

IF WE GO BACK TO 2008, THE FDA PUBLISHED, IN *THE NEW ENGLAND JOURNAL OF MEDICINE*, ON MAY 1ST, 2008 -- THIS IS NOT IN THE RECORD, BUT I CAN SUPPLEMENT OUR RECORD AND GIVE YOU A COPY OF THIS LETTER FROM THE FDA. IT'S WHERE THEY ADDRESS THE CONNECTION BETWEEN THESE DRUGS, EXENATIDE, AND PANCREATITIS. AND THE REPRESENTATIVE FROM THE FDA, A DR. AHMAD, NOTED THAT THE FAERS DATABASE IS, QUOTE, THE MOST COMMON METHOD FOR PHARMACOVIGILANCE FOR NEW AND RARE EVENTS ASSOCIATED WITH THE DRUG.

PANCREATIC CANCER IS COMMONLY DESCRIBED AS A RELATIVELY RARE CANCER. IT OCCURS AT A BACKGROUND RATE OF 12 PER 100,000, WHICH IS WHY NONE OF THESE CLINICAL TRIALS WILL EVER BE POWERED TO SEE PANCREATIC CANCER. NO SUCH CLINICAL TRIAL INDIVIDUALLY WILL EVER BE LARGE ENOUGH TO DO SUCH A STUDY.

DR. MADIGAN, IN HIS MAIN REPORT OF 2012, CALCULATED

THAT YOU WOULD NEED 196,000 PARTICIPANTS TO HAVE SUFFICIENT POWER TO SEE A RISK OF PANCREATIC CANCER.

THEIR OWN RESEARCHER, JOHN BUSE, WHO IS ONE OF THE LEAD RESEARCHERS ON THE LEADER STUDY, I TOOK HIS DEPOSITION. AND I ASKED HIM IF ANY OF THE CLINICAL TRIALS CONDUCTED BY ANY OF THESE COMPANIES WERE POWERED TO SEE A RISK OF PANCREATIC CANCER, AND HE SAID NO.

I ASKED HIM ABOUT THE CARDIOVASCULAR STUDIES: WERE ANY OF THEM INDIVIDUALLY POWERED TO SEE CANCER RISK? HE SAID NO.

I ASKED HIM WHAT WAS HIS ESTIMATE OF HOW MANY STUDY SUBJECTS IT WOULD TAKE TO BE POWERED. HE SAID OVER 100,000.

MY FINAL QUESTION WAS CAN YOU CONCEIVE OF SUCH AN INDIVIDUAL STUDY EVER BEING FUNDED AND CONDUCTED BY ANYONE, EVER? AND HE SAID NO.

WHICH IS WHY WE DID THE META-ANALYSIS, WHICH IS DR. MADIGAN'S MAIN ANALYSIS IN THIS CASE, THE META-ANALYSIS WHERE HE LOOKED AT ALL OF THE CLINICAL TRIALS FROM ALL OF THE DEFENDANTS AND IDENTIFIED EVERY CANCER AND COMBINED THEM AND STILL CONCEDED THAT HIS STUDY WAS UNDERPOWERED BUT SHOWED THAT THERE WAS A POSITIVE ASSOCIATION BETWEEN THESE DRUGS AND PANCREATIC CANCER.

BUT IN ANY EVENT, GETTING BACK TO THE MAY 1ST, 2008 LETTER FROM THE FDA IN *THE NEW ENGLAND JOURNAL OF MEDICINE*, THE RESEARCHER CONCLUDES -- AND I WILL READ IT INTO THE RECORD --

QUOTE, HEALTHCARE PROFESSIONALS SHOULD BE AWARE OF THIS ASSOCIATION AND REPORT ALL SERIOUS ADVERSE EVENTS TO THE FDA OR TO THE MANUFACTURER, CLOSE QUOTE.

SO THIS IS A LETTER TO PRESCRIBING DOCTORS, BASED SOLELY ON SPONTANEOUS ADVERSE EVENT REPORTS IN *THE NEW ENGLAND JOURNAL OF MEDICINE*, SAYING THAT THEY SEE AN ASSOCIATION AND THAT HEALTHCARE PROVIDERS SHOULD BE MADE AWARE OF THIS.

AND WHAT HAPPENED AFTER THIS LETTER? THE DEFENDANT, AMYLIN, SUBMITTED A CBE ADDING A WARNING FOR PANCREATITIS, WHICH IS IN THE LABEL TODAY.

THE COURT: HOW IS THAT INCONSISTENT WITH WHAT THE EGAN REPORT SAYS AT PAGE 795, WHERE THEY SAY ADVERSE EVENTS HAVE INHERENT LIMITATIONS WHEN IT COMES TO PANCREATIC CANCER -- I'M PARAPHRASING -- BECAUSE OF THE LONG LATENCY PERIOD, WHICH IS DISTINCT AND DIFFERENT, WE ARE TOLD BY THE DEFENSE, FROM PANCREATITIS?

MR. DEPEW: YES. AND THAT IS EXACTLY WHY I WAS TALKING ABOUT THIS ISSUE OF WHAT MODE OF ACTION YOU LOOK AT THIS DATA FROM. IF YOU'RE VIEWING THESE DRUGS AS HAVING A MODE OF ACTION OF BEING A DIRECT MUTAGENETIC CARCINOGEN, THEY ARE CORRECT. BECAUSE IF YOU ARE LOOKING AT THAT AND THE INTERVAL OF LATENCY, YOU WOULD THEN GIVE LESS WEIGHT TO THE SPONTANEOUS REPORTING ADVERSE DATABASE.

HOWEVER, THAT IS NOT OUR MODEL, AND THAT IS THE MODE OF ACTION THAT WAS THE POINT OF VIEW FROM THE FDA. THEY DID

NOT -- AND YOU CAN SEE THAT IT'S NOT EVEN DISCUSSED IN THEIR LETTER -- THEY DID NOT ANALYZE THAT DATABASE FROM THE POINT OF VIEW OF WHETHER OR NOT THEY WERE ACCELERATING ALREADY ABNORMAL OR DYSPLASTIC LESIONS.

SO THAT IS THE DIFFERENCE BETWEEN THE STUDY. THEY DIDN'T REALLY LOOK AT IT LIKE THIS WAS AN ESTROGEN THAT WAS ACCELERATING DYSPLASTIC LESIONS AND CAUSING A CONVERSION OF THESE PREMALIGNANT TO MALIGNANT LESIONS. THEY WERE LOOKING AT IT FROM THE POINT OF VIEW OF DO THEY ACT DIRECTLY ON THE DNA AS A GENERALLY UNDERSTOOD CARCINOGEN DOES.

AND THE QUESTION OFTEN IS WHY ARE THESE INCONSISTENCIES IN EXPERTS' ANALYSES? AND THERE WAS A BUNCH OF RESEARCHERS THAT DID STUDIES ON HOW DO YOU UNDERSTAND HOW EXPERTS CAN LOOK AT THE SAME DATA AND HAVE DIFFERENT CONCLUSIONS.

AND I BELIEVE THERE WAS A GROUP OF EXPERTS THAT TRIED TO ANALYZE THIS AND IT WAS CALLED THE DELPHI GROUP. AND THEY PUBLISHED A SERIES OF PAPERS AND THEY DETERMINED THAT ONCE YOU AGREE ON THE QUESTION BEING ASKED, YOU TEND TO GET MORE CONSENSUS AMONG THE EXPERTS. BUT WHEN THERE IS DISCORDANCE OR MISUNDERSTANDING OF WHAT THE QUESTION IS THAT IS BEING ASKED, YOU GET DIFFERING CONCLUSIONS OR ANALYSES OF THE DATA.

SO MY ANSWER IS IS THAT IF THE QUESTION BEING ASKED IS WHETHER OR NOT THESE DRUGS ARE MUTAGENETIC, I CAN UNDERSTAND EXACTLY WHY THE FDA DID WHAT THEY DID. HOWEVER, THEY WEREN'T

ASKING THE SAME QUESTION WE'RE ASKING: DO THESE DRUGS ACCELERATE PROLIFERATION OF PRECURSOR LESIONS AND CONVERT THEM VERY QUICKLY TO CANCEROUS LESIONS.

THE COURT: SO WHERE IN EGAN DOES IT SAY IT'S A MUTAGENIC VIEW OF DATA VERSUS THE CELL PROLIFERATION, OR TO THE EXCLUSION OF CELL PROLIFERATION ANALYSIS? I'M LOOKING AT IT, BUT I'M NOT FINDING IT.

MR. DEPEW: EGAN DOES NOT -- THAT'S RIGHT. IN THE DISCUSSION -- AND I DON'T HAVE THE EXACT SECTION -- WHERE THEY TALK ABOUT THE NONCLINICAL DATA, WHICH WOULD BE THE ANIMAL DATA. ALL OF THOSE STUDIES FROM THE COMPANIES WERE TYPICALLY STUDIES LOOKING AT MUTAGENICITY AND NOT PROLIFERATION. AND I THINK THEY EVEN COMMENT ON THAT. SO IF YOU GO BACK TO THE ACTUAL -- AND WE HAVE DONE THIS. WE LOOKED AT THE STUDY DESIGN.

BUT I WANTED TO ACTUALLY LOOK AT ANOTHER DOCUMENT.

THE COURT: BUT ISN'T IT FAIR TO SAY WE DON'T KNOW THE VIEWFINDER THAT THE FDA TOOK ON THIS QUESTION OF MUTAGENIC VERSUS CELL PROLIFERATING? WE KNOW WHAT SOME OF THE DATA WAS BASED UPON, BUT WE DON'T KNOW WHAT WAS IN THE FDA'S ANALYSIS, OTHER THAN LOOKING AT A CAUSAL RELATIONSHIP BETWEEN INCRETIN MIMETICS AND PANCREATIC CANCER?

MR. DEPEW: LET ME SEE IF I CAN -- YEAH, I SEE THE QUOTE HERE. AND I'M NOT QUITE SURE IT ACTUALLY ADDRESSES YOUR QUESTION. MY CONCERN WAS THAT I DIDN'T SEE THE ANALYSIS, TO

ACTUALLY GO TO THAT LEVEL OF GRANULARITY, WHERE THEY WERE MAKING THE DISTINCTION. ALL I KNOW IS THAT THE STUDIES THAT THEY DESCRIBED, WHERE THEY SAY A POTENTIAL LIMITATION OF THESE TOXICOLOGY DATA LIES IN THE USE OF ONLY HEALTHY ANIMALS -- WHICH IS WHAT, AGAIN, IS NOT OUR CASE -- TO ADDRESS THIS CONCERN, THE FDA REQUIRED SPONSORS OF MARKETED INCRETIN-BASED DRUGS TO CONDUCT THREE-MONTH PANCREATIC TOXICITY STUDIES IN THE RODENT MODEL OF DIABETES.

SO AGAIN, THEY ARE TALKING ABOUT WHETHER OR NOT THESE ACT AS MUTAGENS. THEY WEREN'T SETTING UP, LIKE IN THE GIER CASE, WHERE THEY HAD A KRAS MOUSE ALREADY ACQUIRING THESE LESIONS.

SO THESE ANIMAL TOXICITY STUDIES REALLY WEREN'T DESIGNED TO LOOK FOR WHAT WE ARE GOING FOR AND WHAT I'M SUGGESTING. AND WE KNOW THAT THEY DON'T DISTINGUISH BETWEEN MUTAGENICITY AND NON-CARCINOGENIC MUTAGENS IN THIS LETTER.

THE COURT: THEY DID CALL FOR OR ANALYZE THESE HIGH-FAT FEED DIABETIC RAT MODELS AND COME UP WITH SOME DATA OR ASSESSMENT OVERALL. I MEAN, WE DON'T KNOW WHAT WE DON'T KNOW, AND THAT IS THE TOTALITY OF WHAT THEY DID VIEW. BUT, IN PART, I SEE SOME INDICATION THAT THIS PROLIFERATION -- THAT THE TEST GROUP OF DIABETIC RATS WAS PART OF THE OVERALL INFORMATION THAT WAS BEFORE THEM.

MR. DEPEW: I SAW THAT. THEY DO NOTE PROLIFERATION. BUT, APPARENTLY, THEY GAVE THAT NO WEIGHT. BUT WE DON'T KNOW

WHY, BECAUSE IT'S A BLACK BOX.

THE COURT: WE DON'T, BUT WE DO KNOW IT WAS CONSIDERED AT LEAST IN PASSING BECAUSE IT'S GOTTEN SOME REFERENCE IN THE DATA.

SO I DON'T FIND THIS TO SAY IT'S A MUTAGENIC VIEWFINDER THEY ARE USING. I THINK IT'S REALLY SILENT. WE DO KNOW THERE WERE MUTAGENIC-FOCUSED STUDIES BEFORE THEM. THERE APPEAR TO BE THE RAT MODEL, THE DIABETIC RAT-BASED STUDIES THAT WOULD BE MORE IN THIS PROLIFERATION OR ACCELERATION KIND OF CONCEPT YOU ARE TALKING ABOUT, BUT I THINK YOU ARE FAILING TO CONVINCE ME OF YOUR POINT THAT EGAN NEEDS TO BE TOSSED JUST ON THAT BASIS ALONE.

MR. DEPEW: I THINK ALL I CAN SAY ABOUT EGAN IS I AM LEFT WITH GUESSING WHAT THEY DID, BECAUSE SUMMARIZING THE DATA THAT YOU LOOK AT IS VASTLY DIFFERENT THAN TELLING US HOW YOU LOOKED AT THE DATA, WHAT METHODS YOU USED, AND HOW YOU RESOLVED INCONSISTENCIES OR CONFLICTS. WE DON'T EVEN KNOW HOW THEY VOTED ON IT. DID THEY EVEN VOTE? WAS THE VOTE UNANIMOUS? WAS THE VOTE BY MAJORITY? HOW MANY PEOPLE WERE IN THE ROOM? I MEAN, ALL OF THIS IS A COMPLETE UNKNOWN, WHEREAS WHEN WE GET TO GENERAL CAUSATION IN THIS CASE, WE WILL BE EXPLICIT IN WHAT METHODOLOGY WILL BE APPLIED TO EACH LEVEL OF DATA, WHETHER IT'S CLINICAL TRIALS, OBSERVATIONAL STUDIES, INDIVIDUAL ANIMAL STUDIES OR CASE REPORTS.

THE COURT: BUT FROM WHAT YOU'RE SAYING, YOU COULD

NEVER HAVE PREEMPTION IN A CONTEXT OTHER THAN -- WELL, YOU COULD NEVER HAVE PREEMPTION BECAUSE WE NEVER KNOW WHAT THE FDA IS DOING OR NOT DOING. AND PLAINTIFFS COULD ALWAYS ARGUE THAT THERE IS STUFF THEY ARE NOT SEEING. WE DON'T KNOW WHAT THEY DIDN'T SEE; THEY MAY HAVE MISINTERPRETED. YOU COULD NEVER HAVE PREEMPTION, AND WE DO HAVE IT AS A LEGAL CONCEPT. IT MAY BE RARE AS IT MAY BE, BUT IT EXISTS. SO, YOU KNOW, IT'S THE STRUCTURE OF THE BEAST THAT IS PROBLEMATIC.

MR. DEPEW: I THINK THAT I WOULD BE RELUCTANT TO EXTRAPOLATE WHAT I'M SAYING ABOUT EGAN TO SAY YOU COULD NEVER HAVE PREEMPTION. I THINK THERE ARE CIRCUMSTANCES WHERE IT COULD OCCUR. I THINK IF THEY DID A COMPREHENSIVE REVIEW AND THEY WERE COMPLETELY TRANSPARENT, YOU COULD CONCEIVABLY HAVE IT.

THE COURT: BUT THEY ARE NEVER GOING TO BE COMPLETELY TRANSPARENT. THE FDA IS THE GOVERNMENT. THAT DOESN'T HAPPEN. I DON'T MEAN THAT PEJORATIVELY; IT JUST DOESN'T HAPPEN. THEY WORK IN THE WAY THEY WORK, AND WE GET THE RESULTS. WE GET THE REPORTS. WE DON'T GET ALL THE MINUTIAE THAT WE WANT.

MR. DEPEW: THEY DO OCCASIONALLY PUBLISH FAIRLY EXTENSIVE REVIEWS, AND THEY ACTUALLY HAVE HEARINGS WITH TRANSCRIPTS, WHERE THEY BRING IN EXPERTS AND THEY HAVE TRANSCRIPTS AVAILABLE TO THE PUBLIC. SO THERE IS SOME LEVEL OF TRANSPARENCY THAT I THINK GOES FAR BEYOND THE EGAN LETTER.

THE COURT: IT COULD BE.

ALL RIGHT. WELL, UNLESS YOU HAVE ANYTHING ELSE, I KNOW I HAVE TAKEN YOU PAST YOUR TIME, BUT THANK YOU VERY MUCH.

MS. CROOKE: MIGHT I JUST RESPOND TO THE QUESTION JUDGE HIGHBERGER ASKED, WHICH IS VERY BRIEF? YOU ASKED ABOUT WHETHER WE HAVE A QUESTION OF LAW OR FACT. AND HERE IS WHY I THINK IT'S A COMBINED QUESTION.

BACK IN YOUR COURTROOM, JUDGE HIGHBERGER, A FEW TIMES YOU ASKED US THAT QUESTION: WELL, HOW AM I TO DECIDE THIS? ISN'T IT A FACT QUESTION?

I RAN BACK TO THE BOOKS AND I ADDRESSED IT AT PAGES 11 AND 12 OF OUR BRIEF. WE HAD CARLIN TALKING ABOUT WHY THE MANUFACTURER MUST WARN ABOUT KNOWN AND REASONABLY SCIENTIFICALLY KNOWABLE RISKS, AND CONCLUDED THAT THAT IS NOT INCONSISTENT WITH FEDERAL REGULATORY POLICY. AND THEY SAID THAT RAISES FACT QUESTIONS.

LIKEWISE, *JOHNSON & JOHNSON V. SUPERIOR COURT*, WHICH WAS IN OUR BRIEF, CONCLUDED THAT THERE WERE FACT QUESTIONS IMPLICIT IN THE QUESTION PUT TO THE COURT. AND THAT'S IS WHY I THOUGHT WHEN YOU RAISED THOSE QUERIES TO US AND DID THE RESEARCH, I THOUGHT YOU WERE RIGHT, THAT IT IS ULTIMATELY A FACT QUESTION. IF THE FACTS ARE NOT SUSCEPTIBLE TO OTHER INTERPRETATION, THEN IT'S DECIDED AS A QUESTION OF LAW.

JUDGE HIGHBERGER: THANK YOU.

MR. BROWN: YOUR HONOR, MAY WE HAVE ONE MINUTE TO RESPOND TO SOME OF THE INFORMATION THAT CAME UP THE FIRST TIME?

THE COURT: OKAY. ONE MINUTE.

MR. BROWN: ONE MINUTE. MUCH OF WHAT WE HEARD, YOUR HONOR, WAS PLAINTIFFS' DISAGREEMENT WITH WHAT THE FDA FOUND, BUT THEY DID MAKE REFERENCE TO SEVERAL DATA POINTS, SIX BY MY COUNT.

ALL BUT ONE OF THOSE WERE IN THE PUBLIC DOMAIN WHEN THE FDA MADE ITS CONCLUSIONS. THIS CHAIN ANALYSIS IS THE EXCEPTION. AND WHAT YOU WILL FIND IS THAT CHAIN ANALYSIS ISN'T AN EVALUATION OF WHETHER THERE IS AN INCREASED RISK ASSOCIATED -- INCREASED RISK OF PANCREATIC CANCER ASSOCIATED WITH JANUVIA. THEY WEREN'T ANALYZING THAT AT ALL. WHAT THEY WERE LOOKING AT WAS THE BACKGROUND CHARACTERISTICS OF THE BACKGROUND POPULATION.

AS FOR THE OTHER FIVE -- ELASHOFF, NAUCK AND FENG ARE ALL ANALYSES OF SPONTANEOUS AES, WHICH AS YOU KNOW BY NOW, HAS BEEN EXPLICITLY REJECTED. AND, IN FACT, THE FDA HAS SAID THAT SPONTANEOUS AES ARE NOT A BASIS FOR ANY CHANGES TO THE LABELING.

THE OTHER DATA POINT THAT THEY MENTION, ROMLEY, MR. DEPEW DID POINT OUT THAT THE FINDING WAS NONSIGNIFICANT, BUT I WANTED TO REPEAT THAT. THERE WAS NO SIGNIFICANT DIFFERENCE FOUND IN THAT STUDY.

AND THEN YOUR HONOR HAS ASKED A COUPLE QUESTIONS ABOUT ANIMAL STUDIES. I JUST WANT TO BE CLEAR. TO THE BEST OF OUR KNOWLEDGE -- AND WE HAVE TAKEN A NUMBER OF DEPOSITIONS IN

THIS CASE AND I THINK THIS COLLECTIVE GROUP KNOWS THE DATA PRETTY WELL -- UP UNTIL NOW THERE ISN'T A SINGLE ANIMAL IN ALL OF THE ANIMALS STUDIED IN THE WORLD RELATED TO THIS SUBJECT, THAT HAS BEEN FOUND TO HAVE PANCREATIC CANCER WHILE BEING EXPOSED TO ANY OF THESE MEDICATIONS. THAT INCLUDES LIFELONG CARCINOGENICITY STUDIES THAT WERE DONE AND REFERENCED BY EGAN FOR THESE ANIMALS WHO WERE EXPOSED FOR THEIR ENTIRE LIFE. THEY DIDN'T PRODUCE CANCER. AND I THINK IT MIGHT BE INTERESTING TO NOTE THAT THOSE STUDIES WERE SUFFICIENT, AT LEAST IN LIMITED MODELS, TO SHOW THYROID CANCER IN CERTAIN ANIMAL MODELS. BUT IT DIDN'T SHOW ANY EVIDENCE OF PANCREATIC CANCER.

SO THAT IS ALL I HAVE GOT. I THINK ON BEHALF OF ALL OF US, THANK YOU FOR YOUR TIME.

JUDGE HIGHBERGER: ONE QUESTION. THE CHANG STUDY THAT YOU SAY WAS NOT BEFORE THE FDA, WHICH EXHIBIT WAS IT? I FIND A CHANG STUDY ABOUT TAIWAN, BUT MAYBE IT'S A TIMING QUESTION.

MS. CROOKE: IT'S 27 TO OUR BRIEF.

JUDGE HIGHBERGER: THAT WOULD LOOK TO BE A PUBLIC ITEM FROM THE FACT IT WAS PUBLISHED BY JOHN WILEY & SONS. BUT ARE YOU SAYING, MR. BROWN, IT WASN'T PUBLIC?

MR. BROWN: NO. WHAT I'M SAYING IS MY UNDERSTANDING IS IT WAS PUBLISHED AFTER THE FDA FINDINGS THAT WE HAVE SHOWN YOU. IT'S 2015.

JUDGE HIGHBERGER: SO IT EXISTED IN SOME EARLIER

FASHION, AT LEAST IN MR. DEPEW'S VIEW OF THE WORLD, BUT NOT YET IN THE PUBLIC FASHION OF THE FDA?

MR. BROWN: THAT IS MY UNDERSTANDING. BUT THE POINT I WANTED TO MAKE IS THAT IT'S NOT AN ANALYSIS OF WHETHER JANUVIA INCREASES THE RISK OF PANCREATIC CANCER. IT DIDN'T FIND THAT AT ALL.

THE COURT: WELL, THANKS. THANK YOU ALL VERY MUCH FOR A VERY PRODUCTIVE DISCUSSION. I AM TAKING THE CROSS-MOTIONS IN THE MDL UNDER SUBMISSION AND WE'LL ISSUE, NO DOUBT, A LENGTHY OPINION OF THE FINAL CONCLUSIONS ADDRESSING THE ISSUES PRESENTED. THANK YOU VERY MUCH.

JUDGE HIGHBERGER: SPEAKING AS TO THE COORDINATED PROCEEDINGS, THE MOTIONS TO SEAL ARE NOT YET FULLY BRIEFED, TO MY UNDERSTANDING, OR I CERTAINLY HAVEN'T SEEN THEM IN THE REPLY BRIEFS, SO THEY WILL BE TRAILED TO BE SET SEPARATELY IN MY DEPARTMENT IN LOS ANGELES ON ANOTHER DAY. I AM NOT GOING TO TRY TO FORCE A JOINT HEARING ON THAT, JUDGE BATTAGLIA. I THINK WE CAN DEAL WITH THOSE SEPARATELY, AND THE STANDARDS MAY BE SEPARATE.

COUNSEL IN THE COORDINATED PROCEEDINGS ARE DIRECTED TO OBTAIN A TRANSCRIPT OF TODAY'S ORAL ARGUMENT AND LODGE IT IN DEPARTMENT 32 AT YOUR EARLIEST CONVENIENCE.

I AM WITHDRAWING MY TENTATIVE. THE ORAL ARGUMENT HAS BEEN HELPFUL AND INFORMATIVE. MY MIND IS, AT THE MOMENT, BACK ON A RESET AND I'M TAKING THE MATTER UNDER SUBMISSION, WITH NO

CURRENT INCLINATION ONE WAY OR THE OTHER.

THE COURT: ALL RIGHT. WELL, THANK YOU, JUDGE. THANK YOU ALL VERY MUCH, AND WE'LL BE IN RECESS.

MR. SHKOLNIK: YOUR HONOR, BEFORE THE RECESS, I THINK WE HAD ALSO A CMC SCHEDULED.

THE COURT: A STATUS CONFERENCE?

MR. SHKOLNIK: A STATUS CONFERENCE.

THE COURT: WELL, WE CAN TALK ABOUT THAT. WHAT DO WE NEED TO TALK ABOUT?

MR. SHKOLNIK: YOUR HONOR, I DON'T THINK THERE IS MUCH TO TALK ABOUT, BUT I WANT TO MAKE SURE FOR THE RECORD. (LAUGHTER)

I THINK THE PARTIES NEED TO MEET AND CONFER ON VARIOUS ISSUES FROM THE HEARING THE OTHER DAY, AS WELL AS TODAY'S HEARING, AND I THINK WE WILL BE PROPOSING A FURTHER CONFERENCE.

THE COURT: WHY DON'T YOU CONFER AND LET ME KNOW WHEN YOU THINK OF AN APPROPRIATE TIME, AND THEN YOU CAN SET THE AGENDA. I WILL ISSUE, LATER TODAY, A WRITTEN SUMMARY OF THE FINDINGS OF MY RULING FROM WEDNESDAY. SO YOU WILL HAVE THAT IN SOME CONCRETE FASHION THAT YOU CAN CONFER ABOUT, BECAUSE THAT MIGHT INFORM OR DIRECT YOUR VARIOUS POSITIONS.

SO IS THE DEFENSE COMFORTABLE WITH THE IDEA OF YOU FOLKS CONFER AND TELL US WHEN WE SHOULD SIT BACK DOWN AND TALK STATUS?

MR. KING: YES, YOUR HONOR. THE ONLY COMMENT I HAD -- KEN KING FOR LILLY -- IS AT THE LAST CONFERENCE YOU HAD ASKED THAT WE REPORT ON THYROID CANCER CASES. WE ARE HAPPY TO DO THAT NOW OR AT THE NEXT CONFERENCE.

THE COURT: IS THERE ANYTHING SIGNIFICANT THAT WE SHOULD DISCUSS TODAY, OR WOULD THAT BE ACCEPTABLE TO TRAIL THAT REPORT TO THE NEXT JOINT MEETING?

MR. KING: THAT WOULD BE ACCEPTABLE.

MR. SHKOLNIK: THE SAME FOR THE PLAINTIFFS. AND I DIDN'T STATE ON THE RECORD, HUNTER SHKOLNIK.

THE COURT: I KNOW WHO ARE YOU, BUT FOR THE RECORD.

THE BLACK AND WHITE PAPER DIDN'T, SO THANK YOU FOR DOING THAT. SO WE'LL AWAIT CONTACT FROM COUNSEL AS TO AN APPROPRIATE TIME FOR FURTHER STATUS, AND WE'LL ADDRESS ANY AND ALL ISSUES PENDING AT THAT POINT. SO THANK YOU ALL VERY MUCH AND HAVE A GOOD DAY.

(PROCEEDINGS CONCLUDED AT 12:55 P.M.)

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CERTIFICATION

I HEREBY CERTIFY THAT I AM A DULY APPOINTED, QUALIFIED AND ACTING OFFICIAL COURT REPORTER FOR THE UNITED STATES DISTRICT COURT; THAT THE FOREGOING IS A TRUE AND CORRECT TRANSCRIPT OF THE PROCEEDINGS HAD IN THE AFOREMENTIONED CAUSE ON SEPTEMBER 11, 2015; THAT SAID TRANSCRIPT IS A TRUE AND CORRECT TRANSCRIPTION OF MY STENOGRAPHIC NOTES; AND THAT THE FORMAT USED HEREIN COMPLIES WITH THE RULES AND REQUIREMENTS OF THE UNITED STATES JUDICIAL CONFERENCE.

DATED: SEPTEMBER 15, 2015, AT SAN DIEGO, CALIFORNIA.

S/N_____
JEANNETTE N. HILL, OFFICIAL REPORTER, CSR NO. 11148